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# THE EFFECT OF ZINC PEROXIDE TREATMENT ON ULCERS DUE TO THE MICRO-AEROPHILIC HEMOLYTIC STREPTOCOCCUS

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IN 1935, Meleney (3) established as a clinical entity the chronic, undermining, burrowing ulcers due to the micro-aerophilic hemolytic streptococcus, and demonstrated their favorable response to potent zinc peroxide therapy. The modes of origin (4) of the disease process include the following: First, in incised, infected lymph glands; second, in operative wounds, mostly associated with the intestinal or genital tracts; third, secondary contamination of some pre-existing infection.

The outstanding features of the disease, he pointed out (5), are as follows: (1) That the ulcer may attack any part of the body's surface and any person regardless of age or sex; (2) the micro-aerophilic hemolytic streptococcus is the etiological agent; (3) the lesion is characterized by prolonged suppuration with the development of an ulcer having undermined skin edges, and sinuses burrowing into the deeper tissues which tend gradually to enlarge the ulcer. The base is usually composed of grayish, shaggy, gelatinous granulations. Daughter ulcers are often produced, either by surface inoculation or by burrowing from beneath, and these may fuse with the main ulcer. Muscle and bone are not often affected. (4) Fever and pain with considerable prostration may be present in some cases but entirely absent in others. (5) Treatment with the ordinary antiseptics is usually without permanent effect. The ulcer goes on as an ordinary infection for a time and may show considerable improvement with the treatment used. Ultimately, however, such improvement ceases and the infectious process comes to a complete standstill, or gets worse again, never healing over completely. (6) Properly applied zinc peroxide cream controls the spread of the infection. There are three criteria for success in the use of zinc peroxide: (1) The chemical agent must be potent. Du Pont's "Z.P.O." is satisfactory. (2) The freshly prepared creamy suspension in water must be in intimate contact with all parts of the infected surface. If exposure cannot be obtained by direct application, surgical excision is necessary. (3) The dressing must be effectively protected against evaporation and drying.

Furthermore, as Meleney himself states, little has been recorded in the literature to focus attention on the early diagnosis of these ulcers, so necessary for the institution of proper

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treatment. It is only through the publication of case reports (1, 2, 7, 8, 9) from time to time that the attention of physicians will be directed to this disease when unusual ulcers are encountered.

It is the purpose of the authors of this paper, first, to report 6 cases showing the typical clinical characteristics of chronic, undermining ulcers due to the micro-aerophilic hemolytic streptococcus, observed and treated on the Surgical A Service of the Jefferson Hospital; second, to stress the importance of early diagnosis; third, to urge that anaerobic as well as aerobic cultures be requested routinely on all cases with frank suppuration which fail to respond to ordinary measures; fourth, to record and re-affirm the favorable influence of zinc peroxide on the course of the infection.

The clinical case reports follow:

CASE 1. Reg. No. ZH-5751. E. B., aged 46 years, white female, admitted to the hospital December 14, 1936, discharged February 14, 1937. Result: death.

On May 1, 1936, patient was given a prophylactic typhoid vaccine (T.A.B.) inoculation into the left deltoid muscle. An immediate local reaction followed with abscess formation, which was opened and drained. There is no record of culture having been taken at that time. Frank suppuration was rather slow; nevertheless on June 7 she was told by her physician that the lesion had subsided sufficiently for her to undertake a contemplated voyage to England. She had considerable pain with prostration while en route, the abscess spreading, and she stated that these were the worst days of her illness. During the trip two incisions were made into the infected area. She landed at Plymouth on June 16, with a cellulitis of the left shoulder and upper arm, and was admitted at once to the Prince of Wales Hospital. At this time the wound involved the entire left shoulder down to, but not including, the joint. There were pockets of pus in the peripheral portion of the wound. The skin distal to the abscess was very much darkened and looked as if it would slough. There was no regional lymphadenopathy. The pockets were laid open with free drainage and Carrel tubes were inserted. Continuous Dakin's treatment was adopted. The blood Wassermann was negative. The temperature for the first 2½ weeks varied from 102 to 100 degrees, until July when it commenced to rise, settling down in the next 2 weeks to around 99 degrees again. The pulse was not unduly elevated. Toward the end of July and during most of August, and early in September, there was a tendency to an increasing rise of temperature which slowly and gradually was maintained with an increased pulse rate during September and October. Early in August a pure culture of Staphylococcus aureus was found and a certain number of vaccines were given, but these proved ineffective. No anaerobic cultures appear to have been made. Scarlet fever antitoxin was given in June, likewise nuclein and prontosil tablets, all without benefit.

Three or four operations were performed to open and drain the pockets which had formed from time to time, but in spite of all forms of therapy, the infection spread under the deep fascia, with resulting necrosis. Baths and ultraviolet rays were tried but appeared to irritate rather than to do any good.

Early in November another investigation of the pus was made with the result that hemolytic streptococcus was cultivated, with some colonies of staphylococcus, diphtheroids, and Bacillus proteus. No tubercle bacilli were seen on smear. No anaerobic cultures were done.

X-ray examination of the left arm and shoulder showed nothing abnormal present in the bones.

On December 9, 1936, the patient sailed for America and on December 14 was taken at once from New York to Jefferson Hospital. She was emaciated, sallow, quite prostrated, and was in pain.

*Physical examination.* Over the left axilla, arm, and shoulder, especially posteriorly, the skin and subcutaneous tissues were destroyed and the muscles were lying clearly exposed, with the skin edges undermined and the entire surface of muscles coated with a thick, yellow, purulent discharge. The flaps were undermined and there was a great deal of induration. The elbow was quite stiff while the forearm was edematous. There was some puffiness with discoloration up the neck posteriorly (Fig. 1).

Carrel tubes were placed in the underlying skin edges and the wound was dressed with acriflavine solution. Cultures from the arm on December 18, 1938, yielded Streptococcus hemolyticus, micro-aerophilic, Staphylococcus aureus, Staphylococcus albus, and diphtheroid bacilli. No strict anaerobes were recovered. Two days later, culture of the ulcer revealed Bacillus proteus, Bacillus pyocyaneus, Staphylococcus aureus, and Streptococcus hemolyticus. The blood culture was negative.

The wound failed to respond and on December 28, all the undermined flaps were excised until normal tissue was reached; then the entire ulcerated lesion was covered with zinc peroxide cream, then with gauze soaked in zinc peroxide, and finally with a thick vaselinized gauze and dressings. Dressings were changed daily or every other day. The lesion looked much better though the drainage continued no less copious. However, within a week there was a drop in temperature and pulse. The patient was less toxic and general condition was noted as much improved. The copious discharge continued. At this time the patient developed a pressure sore at the base of the spine. By January 18 the fever had again risen and some edges of the original ulcer showed evidence of beginning spread of undermining. Culture at this time again yielded Streptococcus hemolyticus which was proved to be micro-aerophilic and Staphylococcus aureus. The infection now also involved the

base of the spine with considerable spread and much foul drainage. From this time on, both lesions progressed unchecked. The temperature dropped to subnormal, the pulse continuing around 120. The patient grew gradually weaker and more toxic and died on February 14. Permission for postmortem examination was denied.

CASE 2. Reg. No. AH-4119. A. P., aged 41 years, colored female, was admitted to hospital October 12, 1937, discharged November 24, 1937. Result: improved.

This patient, a very obese colored schoolteacher, came to the hospital complaining of painful ulceration on the outer surface of the right leg just above the ankle, exact duration not known, but probably 3 months. Weight bearing increased the pain. The ulcer had persisted in spite of varied self-medication, and had grown larger, especially during the 2½ weeks prior to admission. She had received no medical treatment.

Physical examination revealed an irregularly shaped ulcer just above the external malleolus of the right leg, with flat edges and discharging sinuses. A thin discharge exuded from a gray surface. The clinical impression was tertiary luetic ulcer.

Cultures on admission October 3, 1937, yielded a hemolytic streptococcus, aerobic, in conjunction with Staphylococcus albus. No anaerobic culture was made. Zinc peroxide treatment was instituted at once. In the interim the blood Wassermann and Kahn were reported as four plus. In addition to the zinc peroxide, she was then placed on mixed antiluetic treatment. The culture on October 14 still showed hemolytic streptococcus and Staphylococcus albus present on aerobic plates. On October 20, 1937, anaerobic culture gave no growth in 48 hours. The wound infection had apparently cleared before the causative organism had been isolated and properly identified. The ulcer healed over quite readily and in 4 weeks had almost closed over completely. The zinc peroxide treatment was discontinued, and warm compresses were applied. No cultures were taken. In another week there was complete closure of the wound by epithelium. Patient was discharged, cured, in care of the physician referring her and he was advised that she had syphilis.

CASE 3. Reg. No. AH-5833. W. L., aged 56 years, white male, was admitted to the hospital December 8, 1937, discharged December 23, 1937. Result: improved.

In February, 1936, the patient sustained trauma to the left forearm just below the elbow. Swelling and ecchymosis followed and receded gradually without treatment. In February, 1937, he noticed over the same area a "boil" which increased in size and later ruptured, draining pus. His doctor used various applications and there was considerable healing of the ulceration with crust formation. The patient then fell and knocked the crust off, and thereafter the ulcer spread with attendant frank suppuration. Subsequently other areas broke out on the forearm, first as abscesses and later as open sinuses. He states that the lesions became intermittently better and worse until 5 weeks prior to admission, when the one on the anterior surface of the forearm began to spread, draining more than before. He gave a history of chancre at the age of 18 years for which he had received some treatment, details not known. Cultures taken in the referring physician's office on December 1, 1937, were reported by the Jefferson Hospital laboratory as "Streptococcus hemolyticus, micro-aerophilic, Bacillus pyocyaneus. No yeasts or molds recovered." Patient sent to hospital because of failure to check spread of the lesion.

Fig. 1. Case 1. Seven months after onset of the disease. Note the undermined skin edges, burrowing sinuses into deeper tissues, daughter ulcers, and bridges of skin. The base is composed of grayish, shaggy, gelatinous granulations.

On admission the left forearm disclosed an area of small burrowing sinuses, extending from the elbow to the middle third of the arm, mainly on the extensor surface, with the exception of one large, punched-out ulcer on the dorsolateral surface. The ulcers had smooth, round, curled edges, presenting a punched-out appearance, with granulating bases. The edges were undermined for some distance back, and some of the ulcers were connected by sinuses. In view of the history of syphilis and four plus Wassermann and Kahn, the diagnosis was tertiary luetic ulcer with the undermining due to secondary infection.

Culture taken on December 9, 1937, yielded no strict anaerobes. The aerobic plates showed Streptococcus hemolyticus and diphtheroid bacillus, unclassified.

The wound was dressed daily with a freshly prepared zinc peroxide cream and sealed off with thick vaselinized gauze. Within a week the ulcers became less inflamed with considerably less suppuration. The

Fig. 2. Case 4. Two and one-half years after onset, showing ulceration of the right arm, involving the entire skin thickness with undermining of the skin edges.

granulations took on a pinkish, healthy appearance. The undermined area filled in and epithelization was in evidence. Cultures on December 17, 1937, yielded Bacillus pyocyaneus, and no anaerobic organisms. By December 23, the healing had progressed so satisfactorily that the patient was discharged in care of the referring physician for continuance of treatment with zinc peroxide, and for antiluetic therapy.

Correspondence with the family physician reveals that the ulcer had become completely epithelized within 3 weeks after discharge from the hospital. The patient is seen weekly for antiluetic treatment by his physician, and there has been no recurrence.

Case 4. Reg. No. ZH-542. H. C., aged 30 years, white female, was admitted to hospital June 15, 1936, discharged June 20, 1936. Result: improved.

Two years prior to admission patient developed an infected hair follicle on the extensor surface of the right arm, just below the elbow. The infection progressed until the abscess attained the size of a lemon, when it was incised and drained. Instead of healing, an ulcer developed and spread until it almost completely encircled the arm, denuding an area 6 to 8 inches wide. Progress from then on varied. At times there was considerable healing, only to be followed by further breakdown. Blood Wassermann taken after a year of various treatments was alleged to have been positive; however, when repeated the report was consistently negative. Nevertheless, two very "sketchy" courses of antiluetic therapy were given, with little change in the character of the ulcer. Roentgen therapy was also tried and had no favorable effect. She was then sent to the hospital, the diagnosis being tertiary lues suspect. No cultures were made.

Physical examination revealed an ulcerated area on the right arm, which almost completely encircled it. It involved the entire skin thickness and was sharply demarcated from the surrounding tissues. The edges were undermined. The raw surfaces were from gray to bright red in color, granular in appearance, and covered with a thin layer of pus. There was no gangrene. A consulting dermatologist made a diagnosis of gumma, and advised local applications of mapharsen, in conjunction with regular antiluetic

Fig. 3. Case 4. Ulceration entirely healed with no undue contracture or fixation of the joint. Through some misunderstanding, views identical with the preceding figure were not obtained.

therapy. The blood Wassermann was negative. The patient was discharged improved in care of the out patient department.

She was readmitted November 16, 1936 (Reg. No. ZH-4987), after a course of bismarsen and iodide therapy, without cure. Repeated serological tests were negative. Lymphopathia venereum was next considered, the Frei test being negative in 24 hours and questionably positive in 48 hours.

Biopsy of the ulcer margin was performed and the diagnosis of "Chronic inflammatory ulcer of the skin; granulomatous type of lesion" made. Various local measures were tried subsequent to this, and antiluetic therapy was continued. Culture on November 27, 1936, yielded Streptococcus hemolyticus and a diphtheroid bacillus aerobically. No anaerobic cultures were taken. She was treated as an out patient from this time until October, 1938.

The ulcer in the meantime had become considerably smaller, only a small area of un-united tissue remaining. This resisted all forms of treatment. In August, 1938, the wound was scratched by the claws of a dog. The ulcer then spread again with copious drainage. Smears were taken from the wound edges and aerobic cultures yielded only Staphylococcus albus. She was readmitted on October 12 (Reg. No. BH-4120) for excision of the infected area (Fig. 2). At this time a request was made for an anaerobic culture of swabs from the ulcer edge, and a growth of hemolytic streptococcus micro-aerophilic, was obtained. The patient was then treated with zinc peroxide. There was a prompt favorable response with diminution in the size of the lesion. She was discharged November 12, 1938, in care of the family physician with a note about the method of treatment, and advice to return to the hospital for plastic surgery if complete epithelization of the wound was followed by limited elbow motion.

Patient was seen February 13, 1939, and there was no recurrence. The wound was completely healed and with no undue contracture nor fixation of the joint (Fig. 3).

CASE 5. Reg. No. AH-9868. J. P., aged 17 years, white male, was admitted to hospital April 27, 1938.

Six weeks prior to admission the patient noticed difficulty in flexing the left knee. A swelling appeared in the popliteal space, and there was some redness and swelling of the posterior aspect of the thigh. On the advice of his physician he applied hot magnesium sulphate compresses. The swelling progressed with increasing pain and fixation of the joint. After 3 weeks the abscess opened and discharged a copious quantity of bloody yellow pus with instantaneous relief. Daily ichthyol ointment dressings were applied for 2 weeks. Instead of healing, the wound continued to discharge and the patient was hospitalized.

Physical examination on admission revealed over the left gastrocnemius muscle an irregular wound discharging thick pus and some blood. The leg was painful on motion. There was a dark, red discoloration of the skin and increased local temperature in the popliteal space. This area was fluctuant and extremely tender. Above it, on the posterior aspect of the thigh, the skin was discolored and indurated. The left inguinal nodes were tender but not unduly enlarged.

Aerobic culture was taken and the Streptococcus hemolyticus and the Staphylococcus aureus were identified. Swabs taken from the margin of the wound 2 days later gave Streptococcus hemolyticus in pure culture. No anaerobic culture was made. Roentgenogram of the bones of the leg was negative.

On April 30, 1938, incision with drainage of the popliteal space abscess was done. Culture was repeated on April 30, 1938, and showed the Streptococcus hemolyticus and the Staphylococcus albus on aerobic and anaerobic plates. A week later the infected sinus was further exposed and drained. Zinc peroxide therapy was then tried. No attempt was made carefully to seal off the cream once applied. The potency of the zinc peroxide was not determined. Complete exposure of the infected area was not effected. The result was unsatisfactory and this form of treatment was abandoned and replaced by hot boric acid compresses. Sulfanilimide was given orally. The temperature for the first 2 weeks fluctuated between 98 and 100 degrees but thereafter was seldom higher than 99.2 degrees. The patient was discharged June 3, 1938, in care of the surgical out patient department, improved, and advised to return daily for re-dressing. At the time of discharge the ulcer was about 9 inches long, and filling in.

However, his next visit was not until June 13, by which time the ulcer had increased in size, with considerable suppuration, and he was readmitted to the hospital, June 15, 1938 (Reg. No. BH-497). Continuous hot boric acid compresses were re-instituted. On culture only a Friedlander bacillus was recovered, and no strict anaerobes. No recheck was made. In the course of a month suppuration ceased, the granulations had filled in most of the ulcerated area to the level of the adjacent skin, and there was epithelization inward from the margins. By July 17, the wound was about half epithelized and patient again discharged in care of the surgical out patient department.

He returned once a week for redressings. Granulation tissue became exuberant and its growth was checked with silver nitrate. He received a course of ultra-violet irradiation with no resultant benefit. Gentian violet, then allantoin, then urea ointment were used but the ulcer did not respond. When the patient returned on November 11, the wound was found very raw, inflamed, foul smelling, and exuding pus. Much of the new skin that had been laid down sloughed off, and re-hospitalization was advised.

On November 16, 1938, he was readmitted for the third time. The wound at this time was very red, indurated, and weeping.

Cultures, taken on admission, for some unknown reason yielded no growth aerobically or anaerobically. Continuous hot compress treatment was instituted. In 2 weeks there was no diminution in the size of the ulcer, so wide excision of scar and indurated tissue was done and an attempt made to close the popliteal space by suturing. Within 2 days, however, there was almost complete destruction of the skin edges, with suppuration, and most of the sutures had pulled out. All sutures were removed and hot compresses were reapplied, until the wound became clean. The edges were very red, blending with a purplish discoloration of the skin beyond. A clinical diagnosis of chronic burrowing ulcer was made at this time, and it was decided to employ zinc peroxide cream. Daily dressings, with the zinc peroxide freshly prepared and well sealed with a thick vaselinized gauze, were begun. Within a week the wound had healed considerably. The purplish discoloration had largely disappeared. The base had taken on a clean, healthy, pinkish granulation and suppuration became progressively less. On December 28, 1938, as no undermining was evident and new skin could be seen to be growing in from the margins, and as it appeared that all foci of infection had been obviated, 15 skin grafts of the Reverdin type were placed on the ulcer bed. All of the grafts were successful. No infection was seen. The patient was allowed out of bed, the knee immobilized by an anterior splint. On January 10, 1939, a slight serous discharge was discovered around the crust surrounding the most distal grafted portion. On lifting the crust, the epithelium around the grafts had broken down, denuding a large area. Cultures were made and yielded a hemolytic streptococcus and Staphylococcus albus, aerobically. No strict anaerobes were recovered. Zinc peroxide treatment was resumed, and in 10 days most of the wound was again epithelized. By February 1 the wound had healed entirely and no further dressings were applied. Patient was discharged, well. He was seen weekly for 3 weeks thereafter. No recurrence.

CASE 6. Reg. No. YH-7469. C. H., aged 53 years, white male, was admitted to hospital February 17, 1936, discharged March 2, 1936. Result: improved.

Three weeks prior to admission, the patient was struck on the right shin, abrading an area about the size of a half dollar. After 2 weeks the spot turned black and a crust formed over it. His physician lifted off the crust and applied an ointment. The lesion then began to extend, and within the next 3 days a punched out ulcer formed which was very painful, especially when the limb was dependent. A cellulitis developed, involving the leg from the toes to the upper third. Several days later he developed chills, fever, and sweating, accompanied by a swollen gland in the right groin. He kept the leg elevated, applying the medication prescribed. In spite of this the ulcer enlarged, exposing the tibia and later the muscles of the calf. A purulent discharge was copious. A small, dusky, bluish area developed just lateral to the ulcer, with perforation from beneath, and extension until it merged with the larger ulcer. The physician then sent him to the hospital.

Examination at this time disclosed a swelling of the right leg, extending from the metatarsophalangeal articulations to the upper third of the leg. This swelling pitted on pressure. The skin was reddened and tender. There was an ulcerated area about 3 inches in diameter and roughly circular in outline, on the anterior surface of the leg, about the middle, exposing the tibia and the muscles of the calf. There was frank suppuration from the base of the ulcer. No cultures were taken at that time. There was a painful, right, inguinal adenopathy. The temperature was 100 degrees on admission and fluctuated between 98 and 101 degrees for the ensuing 4 days. The white blood cells numbered 11,600. Blood Wassermann and Kahn tests were positive.

With the application of hot saline compresses the cellulitis disappeared, and after 2 weeks suppuration ceased entirely, leaving the ulcer base clean and granulating. Gentian violet and tight dressings were applied daily and on March 2, 1936, he was discharged in care of the out patient department where he received ultraviolet therapy by means of quartz bulb.

He was readmitted on May 22, 1936 (Reg. No. YH-10407), with extension of the ulcer downward. Ultra-violet therapy and local applications had been ineffective. The ulcer base was then scarified, and many small pinch grafts were applied. He was discharged on May 31, 1936, improved.

Because the wound began to suppurate, the patient became discouraged and went to a private physician, and was given therapeutic roentgen radiation with no benefit, and loss of the pinch grafts which had apparently taken. The diagnosis of varicose ulcer was then made and a sponge pressure bandage was applied. The ulcer responded well for a time but in a few weeks again began to spread, with suppuration. He was readmitted on July 15, 1936 (Reg. No. ZH-1539). The ulcer now measured 2 by 3 inches and was shallow and not undermining. Continuous hot compresses were applied with beneficial result. The thought that the ulcer could be on a circulatory basis prompted pavaex suction pressure treatment, in conjunction with the application of local antiseptics. Slow healing was noted and the ulcer diminished markedly in size. On September 7, 1936, some inflammation with fluctuation developed at the upper margin, and on pressure pus could be expressed. There is no record of cultures having been taken. Hot saline compresses were not effective and incision with drainage was necessary. Profuse suppuration and irregular temperature elevation persisted for several days, with gradual subsidence and partial healing, until the ulcer became quite small again. He was discharged on December 19, 1936, improved, in care of the out patient department. He was redressed three times weekly. Nevertheless the ulcer started enlarging and he was readmitted February 1, 1937 (Reg. No. YH-7469). The ulcer now measured 7 by 3½ inches, with edges undermining and surrounding tissues dusky and exquisitely tender. The base was grayish with areas of sloughing and there was a mucus-like secretion. Pavaex treatments were again tried in conjunction with the application of azochloramid. Cellulitis of the entire leg followed and was successfully combated by elevation and compressing.

A spinal fluid Wassermann was negative. Aerobic culture from the wound yielded Streptococcus hemolyticus and Staphylococcus albus. No anaerobic cultures were made. Hot compresses were reapplied. A small abscess formed beneath and behind the internal malleolus which was incised and drained. Aerobic culture of the pus yielded Streptococcus hemolyticus and Staphylococcus albus. The compressing gradually cleaned up the wound with resultant slow healing. On April 20, 1937, full thickness skin grafts were planted on the ulcer. Within a few days these appeared infected and sloughed off. With hot compresses the ulcer again became clean. Codliver oil dressings seemed to promote rapid epithelization and gradual healing. The ulcer had all but healed. An elastoplast bandage was applied and the patient was discharged on September 20, 1937.

He was readmitted on October 15, 1937 (Reg. No. AH-4227), complaining of increasing pain over the ulcer site. The ulcer had regressed so much that the tendons were exposed and appeared to be infected. X-ray suggested periostitis of the tibia. No cultures were made. On November 13, block dissection of the ulcer, including the exposed tendon, was done and the leg was placed in a cast. However, the wound continued to slough and 3 weeks later further débridement was performed. Dakinization was ineffective. In spite of two further débridements, the infection continued unchecked and on January 4, 1938, the leg was amputated just below the tubercle of the tibia. Within a short time the stump became infected, which was not halted by irrigation, drainage, and débridement, and it be-

came necessary to reamputate, this time to the level of the supracondyloid area. This wound too became infected within a short time. Culture of the pus showed hemolytic streptococcus and Staphylococcus albus predominant. No anaerobic cultures were made.

After compressing until the wound appeared fairly clean, zinc peroxide emulsified in water to the consistency of a cream was placed in contact with the entire raw surface and a dressing was applied. (No attempt was made to keep the dressings moist; the patient stated that the material would cake hard until it was like plaster. He stated further that change of dressings was very painful.) Such dressings were applied daily for a month. In spite of the fact that no effort was made to seal the wound completely so as to prevent evaporation and in spite of the trauma attendant upon change of dressings, healthy granulations increased and there was considerable epithelization. For the first time a treatment was successful in maintaining a clean wound. At the end of the month's treatment, granulations had filled in the ulcer bed almost completely and only a small denuded area remained. There was no subsequent breakdown and at his own insistence the patient was allowed to go home on September 16, 1938. He was seen at irregular intervals in the out patient department where he was redressed with local antiseptics. He was readmitted on January 16, 1939, with ulceration of the stump through the entire skin thickness. In addition there were two large, shallow, roughly circular ulcers on the flexor surface, edges rolled and somewhat undermined, base covered with pale, rather shaggy granulations. These were within an area of scar tissue equivalent in size to the original area of denudation. This scar tissue was red and not tender. A culture taken from the ulcer edge yielded Streptococcus hemolyticus and Staphylococcus aureus aerobically and no strict anaerobes. The wound was dressed daily with freshly prepared zinc peroxide cream and sealed off with thick vaselinized gauze. Within a week the ulcers were clean and more shallow due to the filling in of fresh healthy granulations, and reduced in size by epithelization from the edges. Undermining was no longer evident. Culture on January 27, 1939, yielded Staphylococcus albus and Bacillus subtilis, aerobic and no strict anaerobes. However, the surrounding scar tissue appeared more injected than normal and therefore the zinc peroxide treatment was continued. By February 10, 1939, the ulcers had filled in almost to the level of the surrounding scar tissue, which was assuming a more pinkish color. There was no exudation whatever from the base.

The patient was discharged at this time with the understanding that he was to return daily for zinc peroxide dressings.

He continued to do well until March 8, 1939, and gradual regression in the size of the denuded areas was noted. On March 8 he failed to appear. It was then learned that the patient was in such financial straits that his entire care had to be assumed by a city relief agency, whereupon he was sent to a municipal hospital for treatment.

## EVALUATION AND SUMMARY

The 6 case abstracts presented are typical of chronic, undermining, burrowing ulcer caused by a micro-aerophilic hemolytic streptococcus. The modes of onset included contamination of a pre-existing skin abscess (Cases 3, 4, 5); skin abrasion (Case 6); and puncture wound (Case 1). In Case 2 the origin of the disease is not certain although infection of a skin abrasion is suggested.

Pre-eminent is the fact that these infections went along for indefinite periods unrecognized as to etiology. The physicians who first saw the patients believed that they were dealing with ordinary slow-healing wounds. The patients were hospitalized only after trial and failure of the customary methods of treatment. The diagnoses were in many cases revised with lack of success with one treatment and substitution of another. Thus, lymphopathia venereum, tuberculosis, stasis, and luetic ulcers were mentioned but later excluded, either by absence of positive evidence or by failure of cure with the usual routine care. Possibly because of the infrequency of case reports in literature, chronic, undermining, burrowing ulcer was in no instance mentioned early as a possible diagnosis. Interestingly enough, in 3 of the 6 cases (Cases 2, 3, 6) the diagnosis of luetic ulcer was made with positive blood Wassermann and Kahn reactions in each as supportive evidence. A fourth patient (Case 4) was treated for syphilis nearly 2 years on the basis of one alleged positive blood Wassermann reaction which could not be confirmed on repetition. The fact that these ulcers may improve temporarily under various treatments is misleading and may tend to delay the true diagnosis.

Obviously, the diagnosis of this disease is difficult without adequate bacteriological aid, which includes facilities for anaerobic as well as for aerobic bacteriology. The invasive organism grows much better anaerobically than aerobically, at least early in the disease, and may be missed entirely on the aerobic plates, especially in the presence of rapidly growing

secondary contaminants. The same holds true in long standing infections in which the colonies of hemolytic streptococci growing on the aerobic plates are few in number. It is essential, therefore, that material from the ulcers be planted immediately on media under anaerobic as well as aerobic conditions. Furthermore, it is practicable to advise the laboratory that a search for micro-aerophilic, hemolytic streptococcus is to be made. Otherwise the information that hemolytic streptococci were present on anaerobic plates might be obscured. Thus, Cases 2 and 6, while presenting a typical clinical picture for chronic undermining, burrowing ulcer, do not have bacteriological proof that a micro-aerophilic hemolytic streptococcus was the etiological agent, in spite of the fact that in certain instances anaerobic cultures were made. For frequently reports of "no strict anaerobes recovered" were returned, stating nothing about the presence of hemolytic streptococci growing on the anaerobic plates and the relative number present in comparison to aerobic plates made simultaneously. The streptococci growing on the anaerobic plates were not routinely tested for micro-aerophilic properties. In numerous other instances no anaerobic cultures were requested. Had more adequate bacteriological studies been made on all of these cases, the likelihood is that an accurate diagnosis would have been possible much earlier in the disease.

To facilitate early recognition of this disease, as well as other types of surgical infections, the following routine has been established in this laboratory:

The swabs are plated on blood agar and glucose agar plates. After the cultures are made, a smear is gram stained to see if organisms are present. One such blood plate is incubated aerobically and another anaerobically. A number of methods are employed for securing anaerobiasis, e.g., displacement of rarefied air in a jar by nitrogen or carbon dioxide; absorption of air from a sealed jar by pyrogallic acid and alkali. Because of its simplicity and ready availability, the Spray dish (10) method is most commonly used. All colonies growing anaerobically are tested aerobically and retested in deep semisolid veal or glucose agar tubes for character of growth. Cultures growing in the top level of the deep agar tubes are called micro-aerophilic. The Spray dish method is satisfactory for routine work and represents a minimal outlay for doing anaerobic bacteriology.

Case 6 is representative of the way these infections may continue for months or years with extensive destruction of tissues before the true cause is recognized. The disease began as a trivial abrasion and spread with involvement of the surrounding skin and subcutaneous tissues until there was extensive destruction. The failure to heal was attributed to the presence of syphilis. When luetic therapy in conjunction with various antiseptics failed to effect a cure, a diagnosis of stasis ulcer was made and adhered to for a long time. The regressions were explained on the basis of secondary infection. Each time that the acute infection would subside, the patient was discharged from the hospital and was treated as an ambulatory case. This happened 6 times.

It was not until the fifth admission that further possibilities were looked into, and this after two amputations and several débridements had already been made. An earlier diagnosis might have been made, had there been (1) true appreciation of the clinical manifestations of this infection; (2) consideration of chronic, burrowing, indolent ulcer in the list of differential diagnoses; and (3) adequate and complete bacteriological studies. If the characteristic features of the disease had been recognized and very careful anaerobic bacteriology had been conducted, it is quite possible that earlier institution of zinc peroxide treatment would have saved this man's limb.

The economic aspect of this case merits consideration:

This patient was a machinist earning $32.00 to $40.00 per week, but at the time he became incapacitated, he had been averaging only 3 to 4 days' work per week. His mean weekly wage on this basis was $24.00 per week. To date he has been idle 157 weeks and his loss of income for that period totals $2,736.00. In the first part of the illness he spent $200.00 of personal savings and members of the family contributed $274.00. He was hospitalized 110 weeks at a cost to the hospital of $2,987.25.

In recapitulation:

| | |
|---|---|
| Patient's wage loss | $2,736.00 |
| Patient's savings used | 200.00 |
| Cost to family | 274.00 |
| Cost to hospital | 2,987.25 |
| Total | $6,197.25 |

The ultimate cost of the loss of the limb and the necessary rehabilitation is difficult to estimate.

The loss of morale observed in each of these cases is noteworthy, as is the intense discouragement due to repeated disappointment in the various treatments.

Concerning treatment, the failure to obtain permanent improvement with ordinary measures, in spite of careful supervision is brought out in the case summaries and serves as the most forceful argument for the urgent need of early diagnosis. Yet when potent, freshly prepared zinc peroxide cream (6) is carefully applied to all affected parts of the wound and the application protected against drying, the effect is dramatic. Within a few days the exudation ceases, granulations start filling in, the undermining becomes less, and the wound takes on a healthy appearance.[1]

Case 1 is of especial significance in its failure to show this typical response. This case illustrates deep invasion into the axilla with involvement of the lymph nodes and undermining of the muscles and tendons. One of the first conditions for the successful use of zinc peroxide is that the preparation must reach all parts of the wound. In this case complete exposure was not obtained in that the muscles and tendons were not severed and the sinuses had burrowed deeply beneath them. These were injected but it is probable that the foci of infection were not reached. This is especially true when the infection invaded the spinal muscles.

The second prerequisite for good results in zinc peroxide therapy is that an effective or potent preparation must be used. When treatment in Case 1 was first instituted, the zinc peroxide employed was a commercial preparation obtained in the open market. When no benefit whatever could be observed from its use, Dr. Meleney was consulted and he forwarded some of the tested material. However, by the time an effective preparation was procured, the destructive process had already spread so considerably and with even deeper burrowing that complete exposure by débridement was impossible. It is quite possible that, had an effective preparation been obtained earlier in the disease and had more attention been paid to the necessity for flooding all affected parts of the wound with the cream, the progress of the ulceration might have been arrested.

[1]Meleney and Harvey, Ann. Surg., 1939, 110: 1067-1094, have found that peroral administration of sulfanilamide in conjunction with the use of zinc peroxide hastens the process of healing in many cases of chronic, undermining burrowing ulcer.

## CONCLUSIONS

1. Six cases have been presented, showing the typical clinical characteristics of chronic undermining, burrowing ulcers due to the micro-aerophilic hemolytic streptococcus.

2. The importance of early diagnosis through recognition of the clinical manifestations, and isolation of the micro-aerophilic hemolytic streptococcus by securing anaerobic as well as aerobic cultures routinely, has been stressed.

3. The cost of delayed diagnosis is illustrated.

4. A simple technique for doing anaerobic bacteriology is suggested.

5. The favorable influence of properly employed zinc peroxide therapy as observed by Meleney, is confirmed.

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# THE CLINICAL USE OF GONADOTROPIC HORMONE FROM PREGNANT MARE SERUM

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THE dominant rôle played by the anterior lobe of the pituitary gland in controlling ovarian activity has been recognized since 1927 when the experiments of Aschheim and Zondek in Germany and of Smith and Engle in this country were published. Until recently, however, no gonadotropic hormone has been available clinically which reproduced the effect of the anterior lobe of the pituitary. The anterior pituitary-like substances from pregnancy urine while of clinical value do not result in normal ovarian stimulation. They do not stimulate follicle ripening or produce ovulation. Their effect is presumably the production of luteinization although this action is not constant in the human subject (Ross and Hamblen, 9). The urine of women in the postmenopausal period contains a different type of gonadotropic substance which in the hypophysectomized rat stimulates follicle growth to the point of maturity but does not result in ovulation or luteinization.

The accumulated evidence suggests that the cyclic activity of the ovary depends upon the concurrent action of the follicle stimulating and luteinizing fractions of the anterior pituitary lobe and that ovulation is the result of a proper balance between these two types of gonadotropic material.

In 1930, Cole and Hart observed that for a short period of time, a gonadotropic substance was present in high concentration in the blood of pregnant mares, reaching a maximum concentration about the seventieth day of gestation. Cartland and Nelson have purified this substance by fractional precipitation with acetone or alcohol, removal of impurities by adjustment of the acidity, and final precipitation in an increased concentration of acetone or alcohol. The purified material is stable as a dry, white powder essentially free of serum proteins, and non-toxic.

The hormone is assayed biologically by a method based upon the increase in the weight of the ovaries in immature rats. One rat unit is the total dose which, administered subcutaneously in daily divided doses to 21 to 23 day old female rats weighing 30 to 40 grams, will produce a pair of ovaries weighing 65 grams. This must be five times the weight of the ovaries of the uninjected control animals. The various authors are not in agreement as to the most accurate method of standardization of gonadotropic hormones. Moricard and Gothié discussed the standardization of pregnant mare serum hormone and have constructed curves showing the relation of the logarithm of the dose to ovarian and uterine weights of mice. They propose two units: (a) the opening of the vagina in 50 per cent of mice; the fivefold multiplication in the weight of the uterus in 10 mice (1$\mu$); (b) constant keratinization of vagina, the fifteenfold multiplication of uterine weight, the threefold multiplication of ovarian weight (10 gamma). Heller, Lauson, and Sevringhaus found that the uterine weight was the most satisfactory end-point.

The hormone may be administered safely either intramuscularly or intravenously. We have routinely tested all patients for protein sensitivity by intradermal injection. One patient developed a skin rash during the course of intramuscular treatments. This disappeared in 4 to 5 days and did not recur during a subsequent course. One patient who received the hormone intravenously exhibited a reaction thought to be psychogenic and it did not recur with later intravenous injections. No other difficulties have been encountered in the course of several hundred intramuscular and intravenous injections.

A number of experiments have been recently reported which indicate that the gonad-

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otropic hormone from pregnant mare serum unquestionably induces growth of ovarian follicles and ovulation. Hartman was able to induce follicle growth and ovulation in a number of monkeys sexually inactive over a period of months. Although his results were far from promising, this was the first time artificial ovulation has been possible in the monkey. More recently, in an as yet unpublished experiment, he induced multiple ovulations in a bitch during the anestrus period and recovered 12 ova from the fallopian tube. He noted that the uterus of the bitch showed little change. This fact would indicate that ovarian stimulation had proceeded so rapidly that the uterine mucosa could not keep pace with these ovarian changes. The author noted this inability of cyclical events to keep pace with one another in previous experiments and remarked that "the production of ovulation does not guarantee an endocrine condition favorable to implantation of the fertilized ovum."

Foster and Fevold studied the follicle stimulating and follicle luteinizing effects of gonadotropic substances. They found that in the juvenile rabbit, follicle stimulating fractions injected subcutaneously produced only follicle growth but with a trace of luteinizing fraction spontaneous ovulation occurred. Increased amounts of luteinizing hormone failed to produce ovulation but resulted in follicle atresia, cystic degeneration, and luteinization. Pregnant mare serum when administered subcutaneously, caused follicle growth but intravenously produced ovulation. Furthermore, when pregnant mare serum was added to the follicle stimulating fraction, ovulation resulted. These experimental observations confirm the dual action of anterior pituitary lobe substance in the production of normal ovulation. The mode of administration and the correct dosage are likewise of the utmost importance in the success of gonadotropic therapy.

Casida brought calves to ovulation by the subcutaneous injection of pregnant mare serum for 6 days. He also produced ovulation by the subcutaneous administration of follicle stimulating hormone for 2 to 6 days followed by luteinizing hormone on the seventh day.

Davis and Koff reported in 1938 the production of ovulation in women by the intravenous use of the gonadotrope from pregnant mare serum. This work has been recently confirmed by Siegler and Fein. Thus, it has been possible for the first time to produce artificial ovulation in the human and in the monkey by gonadotrope stimulation.

These selected references throw considerable light on the action of the gonadotropic hormone from pregnant mare serum. In the first place, it combines in the correct proportions the follicle stimulating and follicle luteinizing actions. In this it resembles the action of the intact anterior pituitary lobe or extracts and implants of the lobe. It probably represents the basic gonadotropic hormone being derived from the serum. The gonadotropic substances in pregnancy urine, in the urine of the postmenopausal period, and from other sources may represent metabolically changed products which have lost some of their activities. Recent progress in the metabolism of the estrogens and progestin would indicate that comparable changes may take place in the metabolism of the gonadotropic substances. Chemical studies of the estrogens have clarified the various estrogenic principles derived from the urine, the serum, the follicle, and other sites. Many of these fractions represent metabolically changed products. Pincus and Zahl found that estrone is converted into estriol under the influence of progesterone. Thus, estradiol is the primary or true ovarian hormone produced in the follicle. Estrone and estriol represent conversion products. Venning and Browne have shown that the breakdown product of progesterone appears in the urine as the biologically inactive substance pregnandiol glucuronidate. It is possible that the urinary gonadotropic fractions represent metabolically changed products and that the serum gonadotropic fractions more nearly represent the gonadotropic principle of the anterior lobe of the pituitary. These and other interesting problems await the isolation of the pure gonadotropic hormone and its chemical synthesis.

The correct mode of administration of this active substance holds the key to successful clinical therapy. The experiments previously cited and numerous others indicate that the amount of hormone, the route by which it is

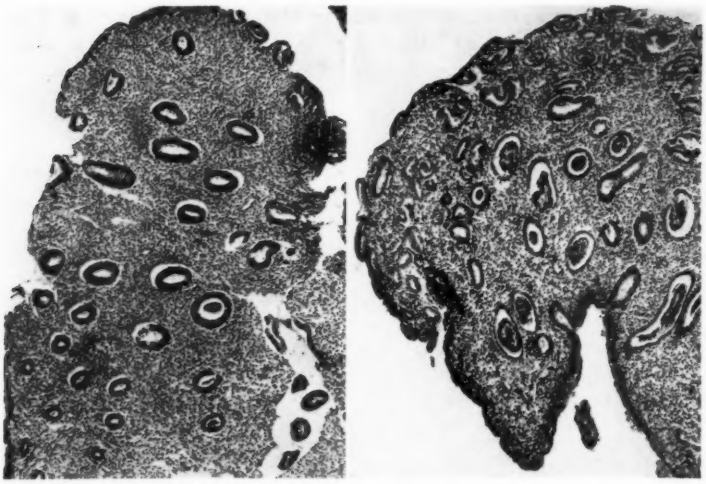

Fig. 1, left. Endometrium 4 days before onset of menstruation shows a proliferative phase without evidence of corpus luteum activity.

Fig. 2. Biopsy, March 14, the first day of a menstrual period, reveals an anovulatory type of endometrium.

administered, and perhaps the proper timing in the cycle may be of the greatest importance. The gonadotropic action of the intact anterior pituitary lobe varies to a considerable extent. It is depleted following coitus in the rabbit and is restored in 24 hours (Friedman and Friedman). Apparently ovulation and depletion of gonadotropic activity in the anterior lobe coincide. These delicate physiological mechanisms are difficult to reproduce artificially and make substitution therapy increasingly difficult.

Were we to have a pure gonadotropic hormone for clinical use we would still have considerable difficulty in developing successful therapy. Too little is known about the endocrine disturbances which lead to a disturbed sex function. The gynecologist is most often confronted only with symptoms in the form of a disturbed menstrual function. Gross examination of the reproductive organs reveals little if any positive information in most instances. The disturbance in physiology may be due to a disordered endocrine balance but that is only the beginning of the problem. The frequency of excellent results with thyroid therapy in some patients with profuse menses and occasionally in patients with amenorrhea is indicative of the importance of the thyroid gland in the endocrine balance of the reproductive organs. The adrenal glands likewise play an important rôle. The amenorrhea of the young woman may not be due to an abnormal anterior lobe of the pituitary gland. It may be due to abnormal reception of the pituitary stimuli as in the presence of refractory ovaries, the absence of normal ovarian tissue or other essential portions of the genital tract.

Careful studies of the cyclical changes in the reproductive organs have correlated the changes in the ovary, the uterus, and the vagina. Thus, the endometrial pattern reflects in a way the stage of follicle development in the ovary and the ovarian changes indicate pituitary function. These endometrial changes represent one way of determining endocrine function. This is a rather crude diagnostic procedure but accurate endocrine assay, particularly for equine gonadotrope, is still clinically impractical. The endometrial picture of ovarian-pituitary function is fairly reliable when typical but it may be less valuable in the borderline problems. It can be said, therefore, that the endometrium mirrors the

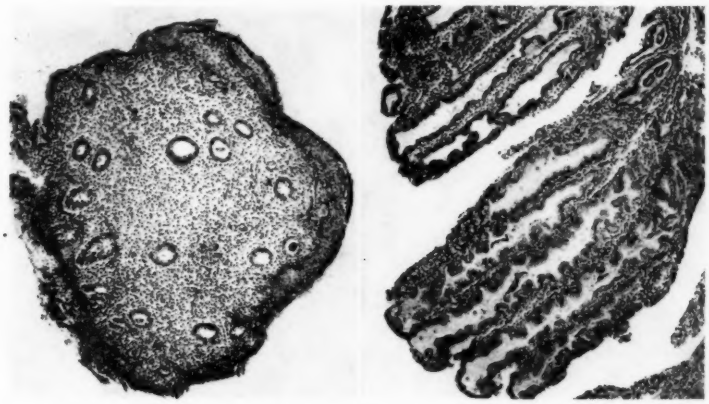

Fig. 3, left. Biopsy of the endometrium taken on October 6 before therapy was instituted on inactive phase. The few small glands are lined by cuboidal epithelium.
Fig. 4. Specimen removed November 9 after gonadotropic stimulation. The endometrium is in the typical late secretory phase.

activity in the ovary and pituitary. The use of frequent biopsies of the endometrium for an evaluation of endocrine problems and therapy has become very popular clinically. It is usually assumed that the proliferative phase of the endometrium represents follicle growth and estrogenic stimulation whereas the secretory phase represents corpus luteum development and progestational stimulation. These latter findings are likewise indicative of ovulation. This indirect evidence of ovulation is the most important clinical evidence available at the present time.

The outstanding discovery of Venning and Browne that the glucuronidate of pregnandiol is a breakdown product of progesterone has provided an additional means of clinical diagnosis. The concentration of this substance in the urine is probably a reliable index of corpus luteum activity. In the absence of ovulation there should be little or no pregnandiol in the urine. It will require considerable evidence to determine the value of the determination of pregnandiol in the diagnosis of endocrine problems.

The selection of patients for gonadotropic therapy should be carried out most carefully in order properly to evaluate the results. Suitable candidates are not numerous if one is to attempt a careful study. During the last 2 years we have accumulated a group of patients in whom pregnant mare serum was used with varying degrees of success. Some of the results were spectacular, others were dismal failures. Our greatest difficulty was the selection of patients in whom gonadotropic therapy was likely to be beneficial.

Sterility patients represent a most interesting group for therapy. However, difficulty arises from the fact that only a small fraction of these women are sterile because of a failure of periodic ovulation. The most careful investigation is necessary to select the few women in whom a lack of normal ovulation is the important factor in sterility. If repeated biopsies before the onset of menstruation or better still, the first day of menstruation to avoid the possibility of disturbing an early pregnancy, fail to show a well developed progestational phase one can assume that the bleeding is anovulatory in origin. Israel and Mazer report that endometrial studies in 36 of 109 regularly menstruating sterile women showed absence of ovulation.

Such sterile patients should be completely investigated to determine the presence of other factors contributing to the failure of conception. Complete general examination of the male partner as well as of the woman should be performed. Local genital tract disease

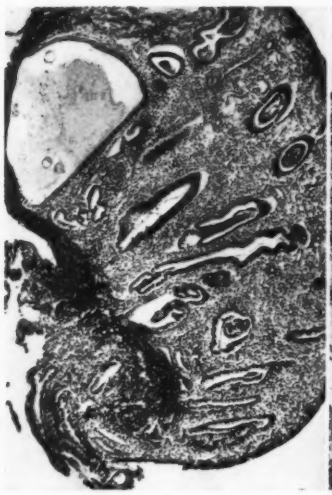

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 5. This specimen of endometrium removed November 3 during the early period of therapy shows a proliferative phase.

Fig. 6. A specimen of endometrium from same patient as in Figure 5 removed 12 days later showing progestation change.

Fig. 7. Biopsy from endometrium of same patient 3 days before next menstrual period shows typical secretory phase.

should be investigated. The presence of normal, active spermatozoa should be established. The patency of the fallopian tubes should be tested. Basal metabolic rate determinations on both husband and wife are indicated.

In this group of sterile patients with failure of ovulation, experimental evidence indicates that the gonadotropic hormone from pregnant mare serum should be given during the late proliferative phase with an abrupt increase in dosage at the time when ovulation might be anticipated. In most instances we have given intramuscularly 20 rat units of the gonadotropic hormone on the ninth, tenth, and eleventh days following the onset of the menstrual period with 60 units intravenously on the twelfth day.

Hartman pointed out the fact that the production of ovulation is not necessarily synonymous with successful implantation of the fertilized ovum. Overstimulation may speed the process so that the endometrial changes fail to keep pace with ovarian activity. Such overstimulation may result in the production of atretic or cystic follicles or the imprisonment and ultimate degeneration of the ovum. That such an event does occur has been amply demonstrated in the experimental animal. Occasionally menstrual bleeding starts several days or even a week early in patients treated with the gonadotropic hormone. This may indicate a disturbed cycle as the result of degenerative changes in the ovarian follicle. It usually is well to wait a month or even two before resuming gonadotropic stimulation.

### STERILITY

The following patients are illustrative of the group of sterile women who have been treated with gonadotropic hormone from pregnant mare serum.

Case 1. R. R. Unit No. 187595. The patient, aged 31 years, complained of sterility for over 10 years. Visualization of the reproductive tract revealed normal fallopian tubes. The uterus was grossly irregular as a result of small fibromyomas of the corpus. A biopsy of the endometrium taken 4 days before the February menstrual period revealed a complete absence of progestational changes in the endometrium (Fig. 1). She received gonadotropic therapy for a period of 5 months. During September she was given 20 units of gonadotropic hormone intramuscularly on the seventh, eighth, ninth, and tenth days of the cycle and 60 units intravenously on

Fig. 8.

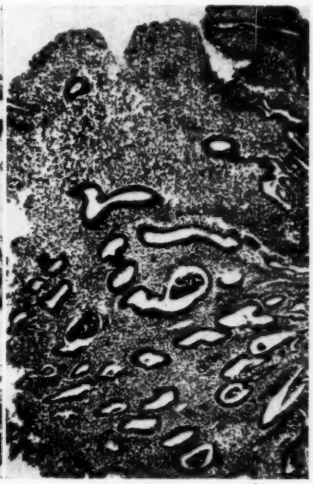

Fig. 9.

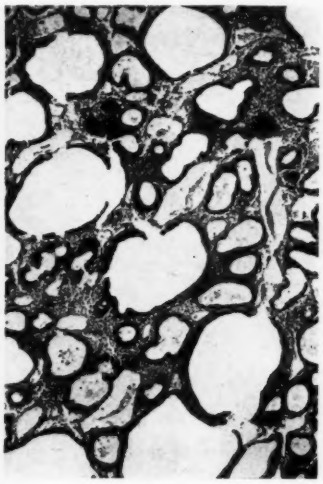

Fig. 10.

Fig. 8. Endometrial biopsy removed on August 31 before the onset of therapy reveals a marked hyperplasia of the endometrium.

Fig. 9. A second biopsy obtained 14 days before onset of a 3 day period in April shows a well developed proliferative endometrium.

Fig. 10. Typical well marked hyperplasia of the endometrium before the onset of therapy.

the eleventh day. No subsequent menstrual periods occurred. She was delivered at term of a healthy baby by cesarean section on May 19, 1939.

CASE 2. E. L. Unit No. 187037. The patient, aged 22 years, was sterile for 2½ years. Her menstrual periods have always been irregular with the interval varying from 28 to 56 days. An endometrial biopsy taken in January on the eighteenth day of a 37 day cycle revealed a proliferative phase in the endometrium with no evidence of secretion. In

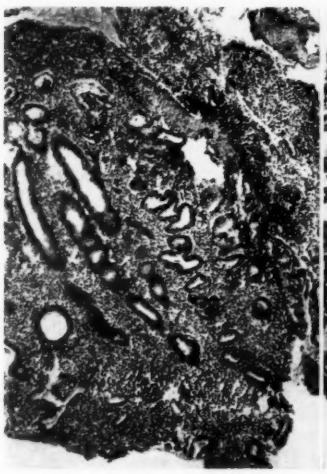

Fig. 11.

Fig. 12.

Fig. 13.

Fig. 11. The initial biopsy specimen of endometrium indicates that the uterine bleeding is probably anovulatory in character.

Fig. 12. Biopsy from the same patient taken 3 days before a period in March reveals a typical secretory endometrium.

Fig. 13. Biopsy before treatment during next cycle shows a very inactive endometrium.

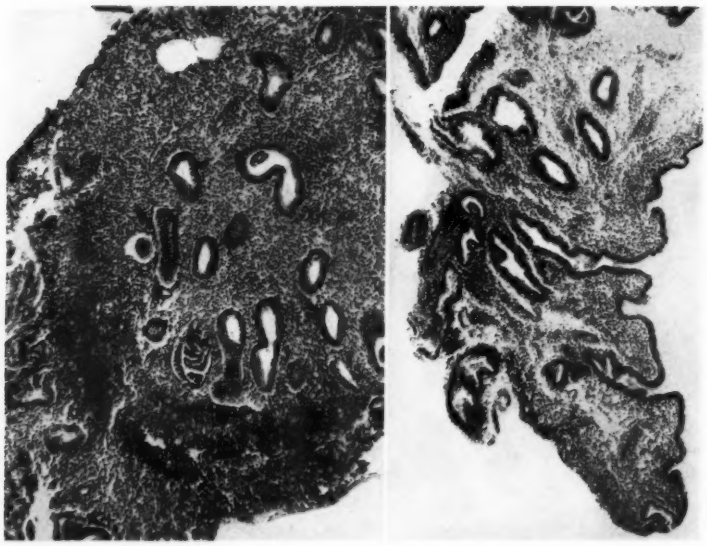

Fig. 14, left. Endometrial biopsy during period of irregular bleeding as described in the text is not associated with ovulation.

Fig. 15. Biopsy 2 days after cessation of normal period in December shows a proliferative phase in the endometrium.

March a biopsy taken during the first day of the menstrual flow revealed a typical proliferative phase in the endometrium indicative of the absence of ovulation (Fig. 2). Given 3 intramuscular injections of 20 units each of gonadotropic hormone, days 8, 9, and 10; intravenous injection of 60 units on day 11. No further periods. Delivered of living baby Jan. 2, 1939.

CASE 3. A. S. Unit No. 184789. The patient, aged 30 years, complained of involuntary sterility for 2 years. She had a single menstrual period at the age of 17 following which she had no periods for 1 year. During the past 10 years her menstrual periods have been very irregular occurring at intervals of from 1 to 8 months. An endometrial biopsy taken in October following an amenorrhea of 7 months revealed a very inactive endometrium (Fig. 3). She had a prolonged menstrual period following 8 daily intramuscular injections of 20 units of gonadotropic principle. She was treated again during the tenth, eleventh, and twelfth days of the next period. An endometrial biopsy obtained on the twenty-third day revealed a typical corpus luteum phase in the endometrium (Fig. 4). Given 4 intramuscular injections of 20 units each during sixth to tenth days of December period. This was the last menstrual period. Delivered prematurely on September 11, 1938.

### AMENORRHEA

Associated with the group of patients with amenorrhea there are a variety of endocrine disturbances representing differing grades of failure in the pituitary-ovarian-uterine complex. Milder degrees of failure may be present in the patient who has occasional spontaneous periods with intervals of amenorrhea which may be long or of relatively short duration. This type of patient should not be considered a true amenorrheic and in most cases menstruates infrequently because of a sub-threshold ovarian stimulation. Stimulation of ovarian activity with equine gonadotrope may be possible. The following is illustrative of such a result.

CASE 4. S. B. Unit No. 186182. This patient, aged 22 years, had had one period during the past year, a scant 3 day flow in March, 1939. There had been no bleeding for 8 months when therapy was instituted. Three courses of intramuscular injections of 20 units of gonadotropic hormone from mare serum were given during successive months. Each was followed by vaginal bleeding of 3 to 4 days' duration which began from 7 to 10 days following the last injection. Endometrium obtained at the onset of treatment (Fig. 5) showed little activity. A biopsy taken 4 days before the onset of bleeding in November revealed a typical secretory endometrium (Fig. 6). Preceding the next menstrual flow the endometrium was again secretory in character (Fig. 7).

In the patients with a more complete amenorrhea we are apt to encounter situations in which the ovary is totally inactive and refractory to stimulation. We may divide these patients into three groups on the basis of their history, physical findings, and from theoretical considerations.

In the first group are patients who have never menstruated and who have failed to develop secondary sex characteristics. In these patients the ovaries have not been stimulated and the genitalia are hypoplastic. If treatment is started shortly after the time when puberty should occur, it may be possible to produce normal development and initiate menstruation. We have been unable to accomplish this result in one patient who has had prolonged treatment.

CASE 5. S. B. Unit No. 150466. The patient, aged 19 years, single, had never menstruated. There was a definite hypoplasia of the genital tract. The uterus was small with a relatively long cervix. Some development of the breasts had occurred. This patient had received various forms of endocrine therapy during the 3 years before she came under our observation. These had included treatment over a 2 year period with thyroxin and theelin. She had also received treatment with prephysin. From March 25, 1937, to May 10, 1937, she received 18 intramuscular injections of 15 units of gonadotropic hormone from mare serum. In August, 1937, she was given 8 injections of 8,000 international units of amniotin in oil, and it was planned to follow these by gonadotropic hormone in the hope that we might in some way produce genital development. She became discouraged, however, and did not report for treatment until 4 months later. During January, February, and March of 1938 she received 4 to 6 intravenous injections of 60 units of gonadotropic hormone from mare serum. We were never able to obtain sufficient endometrium for microscopic study. There was no increase in the size of the uterus and no bleeding. The only subjective symptoms were slight tingling in the breasts on 2 or 3 occasions. She has subsequently been treated by both intramuscular and intravenous administration of the gonadotropic hormone without success.

The second group of patients with amenorrhea consist of those who have never menstruated but do show normally developed secondary sex characteristics. In this way they show evidence of some ovarian activity. These patients may be refractory to treatment, perhaps because of an inability of the ovaries to respond to stimulation. They are not always so, however, as shown by the following record.

CASE 6. R. H. Unit No. 181785. Patient, aged 24 years, has been married 1 year and has had no pregnancies. She had had one 3 day period at the age of 11 years but no bleeding since that time. Treatment consisted of 8 to 10 intramuscular injections of 20 units of gonadotropic hormone each month during 8 months from October, 1937, to May, 1938. On two occasions the gonadotropic hormone therapy immediately followed 160,000 international units and 80,000 international units of amniotin in oil. Bleeding did not result in either instance. Two periods of bleeding did occur during the course of therapy and one period has occurred spontaneously at an interval of 4 months following the cessation of treatment. Endometrial biopsy taken before the onset of treatment showed a simple hyperplasia of the endometrium (Fig. 8). A second biopsy taken 14 days before the onset of a 3 day period in April, 1938, showed a well developed proliferative type of endometrium (Fig. 9).

The third group of patients are those with complete secondary amenorrhea. In many instances the amenorrhea of this type follows a pregnancy. Sheehan and Murdoch have shown that such a syndrome may be the result of necrosis in the anterior lobe of the pituitary gland. When of this type, it is accompanied by asthenia, hypothermia, apathy, and sometimes weight loss. Perhaps more frequent is the type of patient in whom there is a rapid gain of weight dating from parturition or from marriage. These patients are refractory to treatment with the gonadotropic hormone. Three patients who developed amenorrhea following their first pregnancies were treated intensively with mare serum gonadotropic substance. In 1 patient the amenorrhea was of over 5 years' duration and in the other 2 over 3 years. The onset of menstruation failed to occur in all 3 of these women.

### FUNCTIONAL BLEEDING

The last group of patients which we wish to discuss are those who have irregular acyclic bleeding. These are the patients with so called functional bleeding. Functional bleeding in young women probably represents a clinical syndrome in which a failure of ovulation may be an underlying cause. In such cases follicles mature but fail to rupture and release their imprisoned ova. The result is an excessive estrogenic stimulation provided by the unruptured follicles. Irregular and prolonged periods of bleeding characterize this condition.

The endometrial picture is usually typical and consists of an excessively thickened mucosa, often polypoid in appearance with glands which vary in size and shape giving the "Swiss cheese pattern" so well described by Novak. Occasionally the endometrium may be early proliferative in type with little evidence of activity. The absence of secretory manifestations on the part of the epithelium in this hyperplastic endometrium is indicative of a disturbed endocrinal balance.

The therapy of this condition has been largely on an empiric basis. With the advent of purified hormones attempts have been made to develop a more rational therapy. Novak and Hurd have reported some success following the administration of gonadotropic fractions from pregnancy urine. The fact that the human ovary does not respond to these substances would indicate that the good effect could not be ascribed to the correction of the endocrinal imbalance. Progesterone has been used in an effort to substitute for a lack of corpus luteum development in these patients. The lack of striking results is probably due to the fact that simple substitution therapy does not correct the disturbed mechanism for endocrinal control of normal cyclical activity. More recently testosterone propionate has been used in the treatment of functional bleeding. Foss, Gaines, Salmon, and Geist, and a number of others have reported that 300 to 1,000 milligrams per month of the male sex hormone inhibits further bleeding and arrests the endometrium in the early proliferative phase. Larger doses cause varying degrees of endometrial atrophy. Associated with these changes evidences of masculinization occur in the form of an increased hair growth in the male pattern, voice changes, and growth of the clitoris. These undesirable side effects may be temporary but they do seriously interfere with the success of therapy.

Theoretically, gonadotropic stimulation of patients with functional bleeding should lead to the completion of normal follicle growth, follicle rupture, and corpus luteum formation. Such a normal sequence should re-establish regular menstruation. A small group of patients were treated with mare serum hormone with varying results. In a few instances there occurred a cessation of bleeding and a return to normal menstrual periods. As a group, however, the results were far from promising.

Spontaneous remissions are not infrequent in the history of this type of disturbance. The following case reports give evidence of an effect produced by the use of the gonadotropic hormone from mare serum.

Puberty is occasionally complicated by very prolonged and irregular periods of bleeding. Adolescent girls may become exsanguinated as a result of the abnormal blood loss. The endometrial picture is similar to that seen in patients with functional bleeding. These changes are probably the result of prolonged periods of estrogenic stimulation. Adolescence represents a period of endocrine imbalance prior to the establishment of regular cyclical activity.

CASE 7. H. R., aged 14 years. Unit No. 204605. The puberty and first menstrual period began on August 4, 1938. The bleeding continued for a period of 8 weeks without interruption. An endometrial biopsy obtained early in September revealed a marked hyperplasia of the endometrium quite typical of the "Swiss cheese" type of Novak (Fig. 10). The patient received 4 intramuscular injections of mare serum hormone, 20 units each, followed by 2 intravenous injections of 60 units each at intervals of every other day. This treatment was repeated the following month. Bleeding ceased about 10 days after the completion of the first course of injections, following which normal menstrual periods were established and continued.

CASE 8. D. J., aged 26 years. Unit No. 190502. This patient has had irregular periods of bleeding and amenorrhea during the past 4 years. A dilatation and curettage was performed elsewhere in 1935. Regular periods occurred for a few months following this procedure. There was continuous bleeding from September, 1936, to January, 1937, repeated from June to September, 1937, and from November, 1937, to the onset of therapy in January, 1938. An endometrial biopsy taken at the beginning of treatment shows a proliferative type of endometrium with some degree of hyperplasia (Fig. 11). Therapy with gonadotropic hormone from mare serum was given during January and February in 2 courses consisting of 7 intramuscular injections of 20 units each. This was followed by 2 courses of 4 intramuscular injections of 20 units each during March and April. The patient had normal periods during the next 5 months. Biopsies of the endometrium taken during the period of treatment are illustrated in Figures 12 and 13.

CASE 9. E. M., aged 26 years. Unit No. 35428. This patient gave a history of alternating periods of amenorrhea and irregular and prolonged bleeding

during the past 5 years. She had been flowing continuously for 2 months when first seen. During a period of 7 months from October, 1937, to April, 1938, she received 6 courses of treatment with gonadotropic hormone from mare serum. Intramuscular injections of 20 units were given daily over periods of from 10 to 3 days, the number of treatments in any one series being decreased as there seemed to be an approach toward regular cycles. A biopsy taken of the endometrium at the onset of treatment shows a little activity on the part of the endometrium (Fig. 14). The biopsy taken on December 14, 2 days following cessation of bleeding shows an early proliferative stage in the endometrium (Fig. 15). It is apparent from the foregoing that regular cycles were not established although the patient was satisfied that a definite improvement had been produced.

In summarizing this group of clinical observations we wish to make clear that there are many gaps in our attempts to correlate what has occurred with what might theoretically have been expected. We do not wish to give the impression, either, that all of our results have been successful. There have been many failures. We have tried to show the type of endocrine problems in which the gonadotropic hormone from mare serum may be of some use. There is a great deal concerning dosage and the optimum time of administration which remains to be determined. We do believe that this is the most satisfactory gonadotropic hormone at present available.

## CONCLUSIONS

1. The administration of gonadotropic hormone from pregnant mare serum has been followed by pregnancy in previously sterile patients in whom anovulatory menstrual cycles have been demonstrated.

2. This gonadotropic hormone has proved clinically effective in some cases of acyclic uterine bleeding associated with evidence of continued endometrial proliferation.

3. Amenorrhea resulting from inadequate ovarian activity has responded to the gonadotropic hormone from pregnant mare serum by the occurrence of uterine bleeding.

4. No untoward effects have been demonstrated either locally or systemically following several hundred intramuscular and intravenous injections of gonadotropic hormone from pregnant mare serum.

5. Further carefully controlled clinical observations are necessary definitely to establish the therapeutic value and indications for the use of gonadotropic hormone from pregnant mare serum.

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# A COMPARISON OF THE PROTHROMBIN LEVELS OF MATERNAL AND CORD BLOOD AT DELIVERY

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A RAPID clinical method for the estimation of prothrombin was proposed in 1935 by Quick, Stanley-Brown, and Bancroft (6, 7), and in 1936 Warner, Brinkhous, and Smith (14, 15) introduced a quantitative method for the determination of prothrombin. The apparent causal relationship between vitamin K deficiency and prothrombin deficiency on the one hand and between a low prothrombin level and tendency to bleed on the other occasioned new interest in all of the hemorrhagic diseases. Whipple as long ago as 1913 suggested that the cause of the fatal widespread hemorrhages in an infant of 2 weeks was probably an absence of blood prothrombin. In 1937, Brinkhous, Smith, and Warner (1) using their own method found that in 21 newborn infants the plasma prothrombin averaged only about one-quarter that of the normal adult and varied between 14 and 39 per cent of normal. In 1 case of hemorrhagic disease the plasma prothrombin was less than 5 per cent of normal. Employing both the method of Quick and of Warner, however, Owen, Hoffman, Ziffren, and Smith found that in 38 infants the prothrombin by the Quick test was normal but by the Warner test was deficient. At first Quick and Grossman (8) also reported that in infants the prothrombin level determined by their method was not significantly lowered, but in a later communication 3 babies at birth had an average prothrombin level of less than 70 per cent (9). In the case of other infants, a marked drop in the prothrombin level apparently occurred on the second day after birth with a rise on the fifth and sixth days. A similar observation was also made by Owen and his coworkers. At about the same time, Waddell, Guerry, Bray, and Kelly (12), also using the Quick method, reported improvement in the low prothrombin level of 2 infants after feeding vitamin K and later in a study of 20 newly born infants reported evidence suggesting that 10 of these treated with vitamin K had more plasma prothrombin than 10 untreated controls (13). Recently Hellman and Shettles, using the method of Warner, Brinkhous, and Smith, have substantiated the findings of these investigators in that the average prothrombin values in dilution units of 19 full term infants was found to be 22.2. In the case of 9 other infants at varying stages of prematurity, the average value of prothrombin was 8.3. At the time of delivery the prothrombin units of the mothers averaged over 100. They were the first to make a direct comparison of the prothrombin levels between mother and child.

The literature concerning the relation between vitamin K and plasma prothrombin has been well summarized in the recent papers of Smith, Ziffren, Owen, and Hoffman, and of Butt, Snell, and Osterberg.

The data concerning the prothrombin level of newborn infants, therefore, is inadequate and conflicting. For this reason it seemed desirable to investigate the prothrombin level not only in a larger series of newborn infants but also in their mothers at delivery. At the time this work was begun, the report of Hellman and Shettles had not yet appeared.

## METHODS

The prothrombin time, by the method of Quick (6, 7), was determined in the case of 50 mothers and 51 babies (including one pair of identical twins) at the time of delivery and in 32 mothers and 33 babies (including the twins) from 7 to 14 days after delivery. In addition at delivery the volume of packed erythrocytes was measured in the case of 39 mothers and babies. Fetal blood was collected in a paraffin-lined beaker from the placental end of the umbilical cord immediately after its section. Mother's blood at this time and

From the Ayer Clinical Laboratory of the Pennsylvania Hospital.

both mother's and baby's blood 7 to 14 days later was collected by venipuncture in clean dry syringes. All blood was immediately mixed with the appropriate amount of oxalate solution. On each day that tests were made, workers in the hospital were used as normal controls.

In all instances, determinations on plasma dilutions of 100, 50, 25, and 12½ per cent were made in the case of controls, mothers, and babies. Higher dilutions were occasionally necessary for interpolation. The prothrombin values of undiluted plasmas and of those of 25 per cent dilution in mothers and babies were calculated by comparison with the normal controls according to the formula illustrated below:

$X$ = the prothrombin value of unknown expressed in percentage of normal control when

$p, p_1, p_2, p_3$ / $t, t_1, t_2, t_3$ = the percentage concentrations and the coagulation times in seconds, respectively, at increasing dilutions of the normal control plasma and when

$t_x$ = Coagulation time in seconds of the unknown plasma.

When $t_x$ lies between t and $t_1$ then

$$X = p_1 + \frac{p_1(t_1 - t_x)}{t_1 - t}.$$

If e.g. $t_x$ = 16 seconds, then $t, t_1, t_2, t_3$ = 15, 20, 30, 50 seconds, and $p, p_1, p_2, p_3$ = 100%, 50%, 25%, 12½%,

$$X = 50 + \frac{50(20 - 16)}{20 - 15} = 90\%.$$

## RESULTS

The results of these determinations are illustrated in Table I. In the case of the undiluted plasmas, the average prothrombin value of the mothers at delivery was 117 per cent of normal and that of the cord blood was 85 per cent of normal. In the case of the 25 per cent dilutions, however, the values were 140 per cent and 63 per cent of normal, respectively. Since the prothrombin determinations were repeated at 7 to 14 day intervals in the case of only 32 mothers and 33 babies (including the twins), Table II is a comparison of the original prothrombin values at delivery of the same cases which were studied again postpartum. The average values of the undiluted plasmas of these mothers and babies were 107 per cent and 77 per cent and of the 25 per cent dilutions were 133 per cent and 62 per cent, respectively. Likewise, 7 to 14 days after delivery the average prothrombin value with undiluted plasma of the mothers was 102 per cent and of the babies 89 per cent, but with 25 per cent dilutions these values were 127 per cent and 82 per cent of normal, respectively.

TABLE I.—COMPILATION OF DATA OF ALL CASES STUDIED

| | Prothrombin values in per cent of normal control | | | | | | | | Volume of packed erythrocytes in per cent | |
|---|---|---|---|---|---|---|---|---|---|---|
| | At delivery | | | | 7 to 14 days after delivery | | | | At delivery | |
| | Mother | | Child | | Mother | | Child | | Mother | Child |
| | A | B | A | B | A | B | A | B | | |
| Maximum | 300 | 270 | 212 | 108 | 200 | 184 | 150 | 125 | 48 | 65 |
| Minimum | 61 | 64 | 27 | 20 | 55 | 87 | 40 | 33 | 32 | 46 |
| Mean | 117 | 140 | 85 | 63 | 102 | 127 | 89 | 82 | 40 | 55 |

A—Undiluted plasma.
B—25 per cent dilution of plasma

Table I shows also that the average volumes of packed erythrocytes in the case of 39 mothers and babies were 40 and 55 per cent, respectively.

None of the babies after delivery showed any tendency to bleed and only 2 cases (cases 6 and 25) were definitely premature. In one of these the prothrombin level was high and in the other low. No definite correlation was found between the prothrombin levels of individual mothers and babies.

## ANALYSIS OF STUDY

The Quick test in which oxalated plasma is employed is based on the simple concept that

TABLE II.—COMPARISON OF THE PROTHROMBIN VALUES OF THE SAME 32 MOTHERS AND 33 BABIES AT DELIVERY AND 7 TO 14 DAYS POSTPARTUM

| | At delivery | | | | 7 to 14 days after delivery | | | |
|---|---|---|---|---|---|---|---|---|
| | Mother | | Child | | Mother | | Child | |
| | A | B | A | B | A | B | A | B |
| Maximum | 250 | 270 | 175 | 100 | 200 | 184 | 150 | 125 |
| Minimum | 71 | 64 | 27 | 20 | 55 | 87 | 40 | 33 |
| Mean | 107 | 133 | 77 | 62 | 102 | 127 | 89 | 82 |

A—Undiluted plasma.
B—25 per cent dilution of plasma.

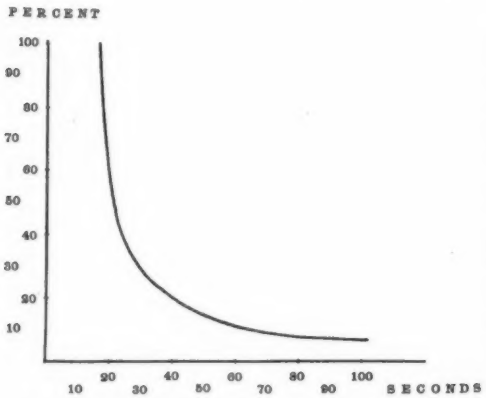


Fig. 1. The average prothrombin curve of 10 healthy individuals (5 men and 5 women). The percentage of plasma diluted with physiological saline solution is plotted against the prothrombin clotting time in seconds. The same thromboplastin solution was used throughout.

blood clotting occurs in two important steps:

1. Prothrombin + thromboplastin + calcium = thrombin.
2. Thrombin + fibrinogen = fibrin.

Since the quantity of plasma fibrinogen would very rarely be altered enough to influence the speed of the reaction and since thrombin probably occurs in stoichiometric proportion to prothrombin, the time required for plasma to clot is largely dependent upon the concentrations of the substances in the first part of the first equation. In the presence of an optimum amount of calcium and of an excess of thromboplastin, therefore, the speed of clotting should indicate the amount of prothrombin. Since the time of the reaction and the amount of prothrombin are not directly proportional to each other, a curve showing serial dilutions of normal plasma plotted against the time in seconds should be constructed for interpolation of the time of clotting of an unknown plasma. Furthermore, this procedure must be done on each day that tests are made since each preparation of thromboplastin will give a different minimum time with normal plasma and since with time the preparation will deteriorate. The absolute time of clotting, consequently, is of no value in determining the amount of prothrombin.

The method of Warner, Brinkhous, and Smith, however, is a much more accurate test for the quantitative determination of prothrombin. These authors have properly criticized the method of Quick in that the test measures not one variable but the sum of two variables because no allowance is made in the first equation for the *convertibility* of prothrombin into thrombin. This difference undoubtedly explains the varying results with the 2 tests given in the literature. Smith and his associates readily admit, however, that the Warner method is too complicated and time-consuming for practical clinical use. They and others have also granted the clinical usefulness of the Quick test and have recently proposed a simpler test than that of Quick for clinical use (11). Even though the Quick test measures the sum of 2 variables, for practical purposes, it does measure the effectiveness of the plasma prothrombin in blood clotting and it has been shown that the results of the test can be accurately correlated with a deficiency of prothrombin and vitamin K. Since the purpose of the present investigation was to determine the relative effectiveness of the prothrombin in fetus, mother, and normal control, the method of Quick was thought to be an adequate procedure.

From a typical composite curve of 10 normal controls (Fig. 1) showing the prothrombin time in seconds at varying dilutions, it is apparent that a slight error in reading the time of the unknown undiluted plasma would make a greater percentage error in interpolation if near 100 per cent plasma than if between 12½ and 25 per cent plasma. Owen, Hoffman, Ziffren, and Smith have also suggested that from Quick's curve dilution should increase the sensitivity of the method. For this reason comparison of the 25 per cent dilutions was made in all cases. It is evident from the results, therefore, that the averages of these dilutions for a series of cases give different results from comparisons of the undiluted plasmas. The tendency for the prothrombin values of the mothers to be above normal and for those of the babies to be below normal is increased in the 25 per cent dilutions so that the average difference of 140 per cent and 63 per cent, respectively, is significant. However, individual cases do not invariably conform with these results. In addition to the

increased sensitivity of the test at these dilutions, it is possible that differences in the convertibility of prothrombin into thrombin, as previously suggested, may be another factor in producing the differences in values.

The criticism may be justly made that the formula used for interpolation of the undiluted plasmas and the 25 per cent dilutions is inaccurate since between dilutions the average percentage value of each second's difference in time is employed when in reality on the curve the percentage value of each second between dilutions varies. An error must, therefore, be introduced in the calculations. In our hands, however, the drawing of the individual curves was thought to be attended by even more error than the use of the formula which was of course more accurate in the range of the 25 per cent dilution than in that of the undiluted plasma.

Furthermore there is no reliable method for estimating the values of prothrombin above normal even with the use of the curve. Since it has been our observation that the time of clotting of some controls as the plasma is diluted tends to increase in rough arithmetic progression, the values of undiluted plasmas above normal have been estimated by reversing this progression. Thus 200 per cent of normal is represented by the time in seconds of the undiluted control plasma minus one-half the difference in time between the control 50 per cent dilution and the undiluted plasma. Such a method is obviously unreliable and the values above normal recorded for the undiluted plasmas, therefore, are at best only rough estimates.

It must also be admitted that another source of error in the test is the use at random of single well persons as controls. Although we agree with Quick that this error is slight, yet a difference between normals of only a fraction of a second makes a large percentage error in the undiluted plasmas. For this reason also a comparison of the 25 per cent dilutions seems preferable to one of the undiluted plasmas. An even better procedure would be to pool the plasmas of several controls.

In spite of these sources of error, however, the fact that the prothrombin values of the infants were so consistently less than those of the mothers and averaged less than those of the controls especially in the 25 per cent dilutions is unquestionably significant. Since the average percentage volume of packed erythrocytes of the umbilical cords was much greater than that of the mothers, moreover, the amount of plasma per volume of whole blood was proportionately less in the case of the babies. The difference in the total prothrombin values for each unit of whole blood must, therefore, be even greater between mother and child than the recorded prothrombin values which have been determined by comparison of equal volumes of plasma.

In some of the cases, determinations of the plasma fibrinogen from the mothers and umbilical cords indicated that in the latter the lowered prothrombin values were not due to a lowering of the fibrinogen. Platelet counts on blood from the umbilical cords in a few of the cases also were normal. More detailed reports of these findings will be made in separate communications respectively by Rush and Hodge.

The results of the prothrombin determinations which were repeated on mothers and babies at 7 to 14 day intervals show little significant change in the case of the mothers and only a slight average increase in that of the babies. Since prothrombin tests were not done on infants between the time of birth and 7 days after delivery, no evidence was obtained as to whether a fall in the prothrombin values occurs in the interval.

None of the mothers received any vitamin K, except in their normal diets, and none of the infants were treated with vitamin K. The elevated prothrombin values of the mothers, however, would not suggest that a deficiency of vitamin K at term was usual.

## SUMMARY

1. The average prothrombin values of 50 mothers and 51 babies at delivery by the Quick test were found to be above normal in the mothers and below normal in the babies.

2. Repetition of the tests 7 to 14 days after delivery in 32 mothers and 33 babies showed no significant change in the prothrombin values of the mothers and only a slight increase in those of the babies.

3. The average volume of packed erythrocytes was much greater in the case of 39 babies than in their respective mothers. The discrepancy between the prothrombin values of mother and child must, therefore, be proportionately larger for whole blood than for plasmas.

4. The Quick test is thought to be a reliable clinical procedure, but sources of error in the method are discussed.

5. It is suggested that comparison of the 25 per cent dilutions of unknown and control plasmas gives more reliable determinations than comparison of the undiluted plasmas.

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# LUNG ABSCESS

## An Analysis of the Massachusetts General Hospital Cases from 1933 through 1937

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IN 1925, Lord gave the results of an analysis of 227 cases of lung abscess observed between the years 1909 and 1924 at the Massachusetts General Hospital. A similar study was presented by King and Lord in 1934 based upon a series of 211 cases recorded between the years 1924 and 1932. The present study is based upon the group of cases observed during the 5 year period, 1933 to 1937, inclusive. Since the last mentioned report there have been certain important changes in our experience with the disease. The x-ray studies have become so accurate that the exact location of the abscess has been designated in every case. There has been a tendency to operate earlier in the course of the disease as well as an increase in the percentage of patients operated upon. Furthermore, the technique of the primary drainage operation has been perfected and improved considerably over that used in the earlier series of cases. There has been a slight but definite improvement in the mortality and a large improvement in the recovery percentage figures with a definite lowering of the operative mortality. Several methods of treatment, such as artificial pneumothorax, extrapleural thoracoplasty, and cautery lobectomy, have been abandoned or at least used very infrequently. On the other hand, primary lobectomy by the improved technique now available has begun to be used, and the number of ultimate cures has been increased by the performance of a lobectomy in certain cases in which simple drainage has failed.

In this series a detailed analysis of every aspect of each case has been made, and it is felt that the statistics presented are as nearly accurate as one can obtain. One hundred and twenty-five cases have been studied and information concerning the end-result obtained in all but 1 (or 124 cases). Certain data such as age and sex incidence are omitted as being of no practical significance.

*Scope.* It must be understood first of all that this report includes all cases of putrid lung abscess whether acute or chronic in which patients were admitted to the hospital during the 5 year period studied. It gives, therefore, the results of our complete experience with the disease during this time.

*Definition of lung abscess.* In going through the record files of the hospital a large group of cases was discovered in which the diagnosis may have been uncertain or confused with some other condition, such as bronchiectasis. These were excluded. The only cases presented here are those in which the patient presented a characteristic clinical history, a foul sputum, and a definite x-ray diagnosis with a cavity and a fluid level. In many, a positive anatomical diagnosis was made at operation or autopsy. For the purpose of this study it is proposed to define an acute abscess as any which has been in existence 4 months or less. Those which have gone more than 4 months are called chronic abscesses. The basis for this division will be discussed (see Chart 6). It is to be clearly understood, however, that this arbitrary definition of the stage of the disease bears no relation to the problem of early versus late drainage which is to be discussed fully under the proper heading.

### PREDISPOSING FACTORS

*Antecedent disease.* In general the otolaryngologists have been disinclined to admit that a large number of cases of lung abscess follow tonsillectomy and other operations on the upper respiratory tract. Table I, however,

From the Thoracic Clinic of the Massachusetts General Hospital.

TABLE I.—ETIOLOGY OF 125 CASES OF LUNG ABSCESS

| | No. cases | Total cases |
|---|---|---|
| Operations in the mouth or upper respiratory tract— | | |
| Tonsillectomy | 54 | |
| Other operations on the nose and throat— | | |
| Repair of harelip | 1 | |
| Radical antrum | 1 | |
| Submucous resection | 1 | |
| Excision of nasal polypi | 1 | |
| Excision of nasal hemangioma | 1 | |
| Radium to larynx | 1 | |
| Peritonsillar abscess | 2 | 8 |
| Tooth extraction | 8 | 70 |
| Various other operations— | | |
| Herniorrhaphy | 1 | |
| Amputation of finger | 1 | |
| Posterior gastro-jejunostomy | 2 | |
| Subtotal gastrectomy | 1 | |
| Hysterectomy | 1 | |
| Cesarean section | 1 | |
| Appendectomy | 3 | |
| Cholecystectomy | 1 | |
| Nephrolithotomy | 1 | |
| Flap operation for varicose veins | 1 | |
| Mastoidectomy | 1 | 14 |
| Normal deliveries | | 4 |
| Aspiration of foreign bodies | | 5 |
| Antecedent pneumonia, "cold," or "grippe" | | 19 |
| No apparent cause | | 13 |
| Total | | 125 |

demonstrates that of 125 cases 54, or 43.2 per cent, followed soon after a tonsillectomy and 70, or 56 per cent, of the cases had either tonsillectomy or some other operation in the mouth, nose, or throat. Only 14, or 11.2 per cent, of the cases followed an operation on some other portion of the body. A few followed normal deliveries or aspiration of foreign bodies. Nineteen, or 15 per cent, followed an upper respiratory infection or pneumonia, and in 13, or 10.4 per cent, no antecedent cause was ever found. In the main, these figures agree with those of King and Lord who found 55.7 per cent of cases preceded by upper respiratory tract operations and 38.6 per cent following tonsillectomy.

## FACTORS INFLUENCING THE PROGNOSIS OF LUNG ABSCESS

By a careful detailed study of these 125 cases certain facts regarding the prognosis become clear.

*1. Duration of disease before entry.* The patients in this series first came to the hospital for treatment at all stages of the disease. By referring to Chart 1 it becomes apparent that relatively few of our operative cases were seen early in the progress of the disease. For reasons to be explained presently, the end of the fourth month of the disease has been designated as the dividing line between what may be called an acute and a chronic case. Taking this as the criterion, it is noted that of those patients subjected to drainage, 37 cases, or 47.4 per cent, were acute and 41 cases, or 52.6 per cent, had progressed to a point where they must be classified as chronic before the patients applied for aid. Throughout the ensuing discussion, however, except in specified instances, no distinction is made.

*2. Period of observation in hospital before operation.* As a working basis in the management of these cases the policy of the thoracic clinic has been primarily to decide on the merits of each case just what should be done, but in general after the expiration of 3 months from the time of onset of the disease the chance of spontaneous cure has been considered to be minimal. Our actual experience has in general supported this belief, although the time must be extended to 4 months instead of 3 (Chart 2). It will be seen from Chart 2 that when operation was performed, the majority of operations were carried out within the first 4 weeks of observation (59 in all). It is apparent, then, that although our clinic has been regarded as following a decidedly conservative course, we have actually operated upon about 73.3 per cent of the cases within 4 weeks of their entry to the hospital, and of these 21, or 35.5 per cent, were operated upon within 8 weeks of the onset of the disease. Making allowance for the fact that a large percentage, approximately 52.6 per cent, of our cases are already chronic when first seen, the number of early operations, i.e., those done within the first 2 months of the disease, compares favorably with the statistics of the advocates of early operation (Chart 3). (See Neuhof.)

The present tendency seems to be to consider 6 weeks from the time of onset as the dividing line between an early operation and a late one. Our experience, however, has been that very few of our patients come to us

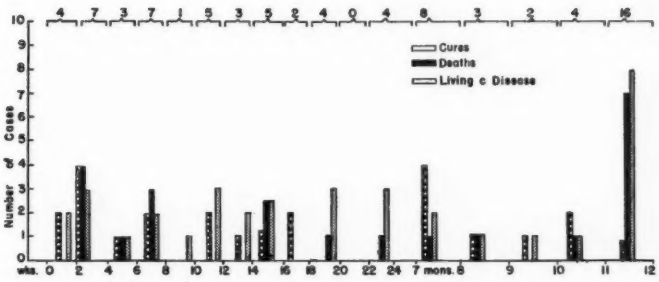


Chart 1. Elapse of time from onset to date of entering hospital in 79 patients operated upon.

promptly enough for us to perform an operation so early. In our group of cases only 8 patients were sent to the hospital soon enough after onset for drainage to be carried out before the end of the sixth week. One observes, therefore, that in the majority of cases the delay in instituting early drainage has occurred before the patient came to this clinic. That there has been little delay after arrival at the hospital is shown by the fact that of the 79 drained cases 38 were operated upon within 2 weeks from the time of their admission to the hospital and, as noted, 59 within 1 month from the time of entry (Chart 2). In the majority of these cases the interval of time between admission and operation was used for diagnostic study and investigation to determine the probable prognosis and the necessity for surgery.

*3. Virulence of the infection.* The severity of the disease seems to vary from patient to patient corresponding in some little understood way to the variation in the virulence of the organisms and the resistance of the patient. In certain patients the course is unusually benign, some of the spontaneous cures having occurred within a few weeks from the onset. Many of the cures reported after routine early operation may very well be in patients of this type who might have recovered even if not operated upon. On the other hand, some of the patients run an unusually fulminating course. For example, of the 14 cases in which death occurred without operation, 10 died in less than 2 months after the onset of the disease. Many other patients with virulent conditions were subjected to operation and, true to its persistently severe

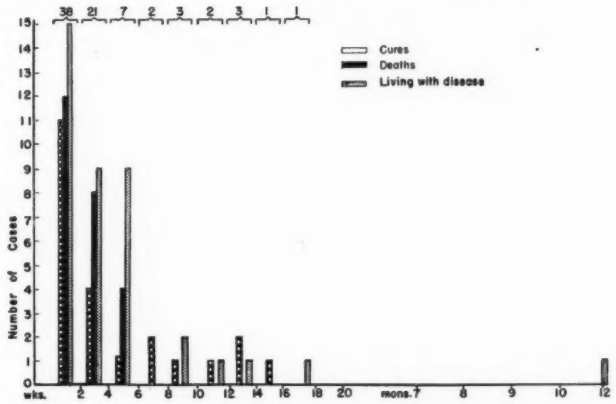


Chart 2. Time: date of entry to date of operation. Period of observation before operation in 79 patients subjected to surgical drainage.

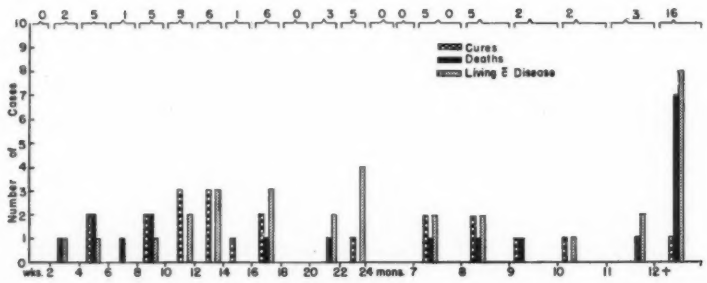


Chart 3. Elapse of time. Onset of disease to date of operation in 79 patients operated upon.

nature, the disease went progressively on, often in spite of multiple operations, to a fatal termination.

*4. Location of the abscess in the lung.* King and Lord state that "a location at or above the root of the lung is relatively favorable while lesions below this level are less promising." This is based on the cases occurring before the more frequent use of lateral exposures made the x-ray localization of the disease so much more accurate. In each of the 125 cases in this present series the anatomical location of the abscess in the lung was accurately determined. In Charts 4 and 5 figures are given to show the numbers which occurred in the apical and lower portions of the right and left upper and lower lobes as well as the right middle lobe. By comparing Chart 4, which presents the location of all the abscesses in the group, with Chart 5, which gives the distribution in the group of patients who were cured spontaneously, one must conclude that there is no significant correlation between the location of the abscess in the lung and the tendency to spontaneous cure.

*5. Prognosis in relation to the stage of the disease (Chart 6).* It would seem to be apparent on the basis of this series that about 49.2 per cent of patients with lung abscess may be cured; that 33.9 per cent die; and that about 16.9 per cent remain alive with disease in spite of treatment. These figures are based upon the experience of our entire group of 124 completed cases. If, on the other hand, the stage of the disease is taken into account, one sees immediately that the prognosis varies from month to month as the disease advances. The importance of more exact knowledge about the prognosis at different stages of the course of the disease is manifest especially

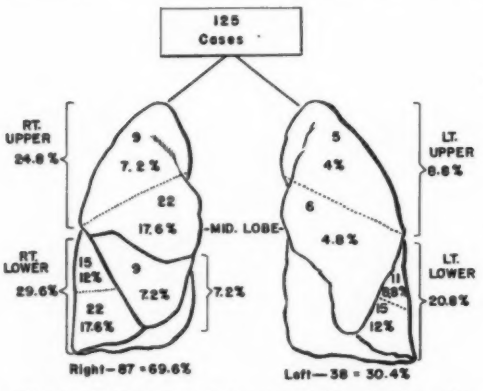


Chart 4. Distribution of abscesses in lung—entire series of 125 cases.

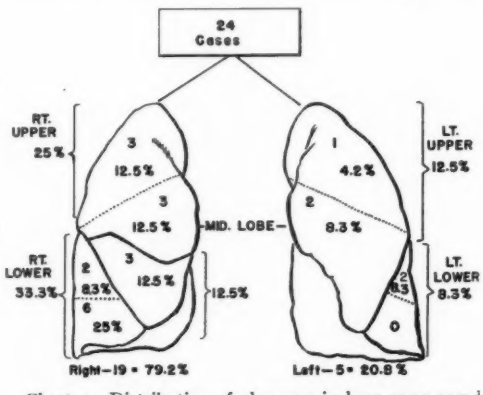


Chart 5. Distribution of abscesses in lung cases cured spontaneously.

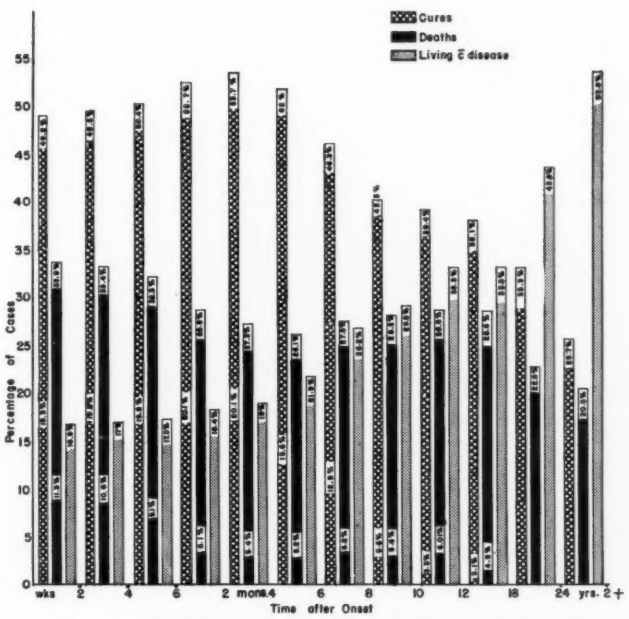


Chart 6. Illustrating the prognosis of lung abscess at various stages of disease from onset to the end of 2 years—Massachusetts General Hospital experience with 124 patients.

during the early months when the decision about whether to operate or not is so difficult and so important. Obviously if there is still a good chance of spontaneous recovery, operation should be avoided. But if one can be reasonably certain that spontaneous recovery will not occur, then the sooner an operation is performed the better the chance of cure, the shorter the period of hospitalization, and the smaller the number of complications. This variation of outlook in relation to the passage of time after the onset of the disease is shown graphically in Chart 6. This chart begins with the percentage probabilities of the entire group of 125 cases. Reading from left to right the figures change as a correction is made for each period of time elapsed. In this way from week to week and month to month a new set of percentage probabilities is given as allowance is made for cases dropped out of reckoning because of deaths or cures.

The cases are grouped under the headings of *those who were cured, those who died,* and *those living with disease after treatment,* with a differently marked block on the chart for each. On the block representing the cured cases, the percentage of expected cures is given at the top: in the lower part of this same block at a proper height is the figure for the percentage of spontaneous cures. Likewise in the block representing the deaths, at the top is given the total percentage of probable deaths for each period and near the bottom of this block is the figure representing the percentage of deaths expected to occur before an operation could be performed. In the third block, at the top is given the percentage of patients expected to be living with disease in relation to each total group. The grand totals naturally diminish from period to period. All these figures, of course, are based on the actual records of the entire group.

As an example of the way in which this chart is intended to be used, let us postulate the case of a patient who has an abscess of 7 months' duration. Such a patient has sur-

TABLE II.—STATISTICAL BASIS FOR CHART 6

| Stage of disease | Cured | To be cured | Cured spontaneously | To be cured spontaneously | Cured by surgery | To be cured by surgery | Died | Left to die | Died before operation | Left to die before operation | Died after operation | Left to die after operation | To remain alive with disease | Total 100 per cent 124 cases |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 to 2 weeks | 0 | 61 | 0 | 24 | 0 | 37 | 1 | 42 | 1 | 14 | 0 | 28 | 21 | from 124 take 1 |
| 2 to 4 weeks | 0 | 61 | 0 | 24 | 0 | 37 | 2 | 41 | 2 | 13 | 0 | 28 | 21 | 123– 2 |
| 4 to 6 weeks | 1 | 61 | 1 | 24 | 0 | 37 | 6 | 39 | 4 | 11 | 2 | 28 | 21 | 121– 7 |
| 6 to 8 weeks | 1 | 60 | 1 | 23 | 0 | 37 | 3 | 33 | 1 | 7 | 2 | 26 | 21 | 114– 4 |
| 2 to 4 months | 9 | 59 | 7 | 22 | 2 | 37 | 5 | 30 | 0 | 6 | 5 | 24 | 21 | 110–14 |
| 4 to 6 months | 13 | 50 | 5 | 15 | 8 | 35 | 3 | 25 | 1 | 6 | 2 | 19 | 21 | 96–16 |
| 6 to 8 months | 7 | 37 | 6 | 10 | 1 | 27 | 2 | 22 | 1 | 5 | 1 | 17 | 21 | 80– 9 |
| 8 to 10 months | 4 | 30 | 2 | 4 | 2 | 26 | 1 | 20 | 0 | 4 | 1 | 16 | 21 | 71– 5 |
| 10 to 12 months | 2 | 26 | 0 | 2 | 2 | 24 | 1 | 19 | 1 | 4 | 0 | 15 | 21 | 66– 3 |
| 12 to 18 months | 8 | 24 | 2 | 2 | 6 | 22 | 7 | 18 | 3 | 3 | 4 | 15 | 21 | 63–15 |
| 18 to 24 months | 8 | 16 | 0 | 0 | 8 | 16 | 3 | 11 | 0 | 0 | 3 | 11 | 21 | 48– 9 |
| 2 yrs. to end of series (i.e., 10 yrs.) | 10 | 10 | 0 | 0 | 10 | 10 | 8 | 8 | 0 | 0 | 8 | 8 | 21 | 39–18 |
| End-result | 61 | 0 | 24 | 0 | 37 | 0 | 42 | 0 | 14 | 0 | 28 | 0 | 21 | alive with disease |

vived beyond the period when some with the severest disease will already have died and has also gone beyond the time when some of the more favorable ones will have been cured. The outlook is obviously different, therefore, from what it would be at the outset. By referring to Chart 6 we learn that this patient has a chance of cure as follows: 46.3 per cent with or without surgery, 12.5 per cent without surgery; a 27.5 per cent chance of death with or without surgery; 6.2 per cent chance of death without surgery; and a 26.2 per cent chance of survival with persistent disease.

Certain interesting deductions can be made from this chart. It is obvious, first of all, that the outlook for spontaneous cure remains about the same, approximately 20 per cent, during the first 4 months after onset, but falls off rapidly from that time until after the expiration of 1 year from onset, when no case can be expected to recover without the benefit of surgery. From this we have come to define any case of lung abscess as acute up to the end of the fourth month, during which time the majority of spontaneous cures may be expected to occur. After 4 months the cases should be regarded as chronic and reasonable expectation of spontaneous cure abandoned. The majority of deaths in the non-operated upon group occur in the early months, but as would be expected, deaths in untreated cases may occur for a considerable period after onset. Another interesting fact is that even after the passage of 1 year or more there is still from 25 to 35 per cent chance of cure by surgical means. Furthermore, of the 21 patients living with disease at the end of the period of observation, only one had not been operated upon one or more times.

For the benefit of those who might be interested to determine how the percentage figures which appear in Chart 6 were arrived at, the actual figures have been arranged in columns and are presented in Table II.

### TREATMENT

Chart 7 summarizes the results obtained in the entire group of 124 patients whose cases were followed to completion. From this one will observe that 61, or 49.2 per cent, were cured, 42, or 33.9 per cent, died, and 21, or 16.9 per cent, remained alive with disease. These terms must be more carefully defined. No case in this entire study has been called cured unless the patient has remained symptom-free for 2 years or more with essentially normal physical signs and the demonstration of healing by x-ray. Many writers on the subject of lung abscess have been content to classify the cases of patients who have not

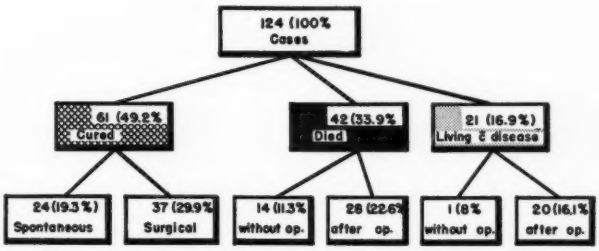


Chart 7. Total experience of 124 patients with lung abscess including all methods of treatment.

died or have been cured as "improved" or "not improved." This is unnecessarily complicated and may lead to a false impression. All those called improved are in constant danger of re-activation and from the standpoint of the result of treatment are no better off than any other uncured case. It seems to be time to abandon this classification and admit that if a patient cannot be called cured according to the aforementioned criteria, he remains uncured. All such cases have, therefore, been grouped under the heading of those who have survived but still have disease. In this group have been placed many who appear on superficial examination to be cured, but who have a persistent or recurrent cavity by x-ray. Some of these were once thought to be cured, but have had a recurrence during the period of observation (2 years or more).

*Medical treatment.* Non-surgical treatment at the Massachusetts General Hospital has consisted of bed rest, attention to nutrition, general supportive treatment, postural drainage, and transfusion if indicated because of anemia. The use of neoarsphenamine has been abandoned. Bronchoscopy was used as a method of treatment in only 1 case in this series and that patient was later operated upon and cured surgically. Twenty-four, or 19.3 per cent, patients recovered without surgery.

*Surgical treatment.* Chart 8 illustrates the experience with surgery in the group of 85 patients treated by operation.

The technique of the drainage operation has been improved since the previously reported series. In the majority of cases the two stage operation has been chosen and performed as follows:

Local and regional anesthesia with procaine hydrochloride is used. After choosing the most direct approach to the region of the abscess, a long incision is made usually parallel with the underlying ribs which are exposed and freed of their periosteum along about 4 to 5 inches of their lengths. If the localization has been accurate the lung and pleura are almost always found to be adherent. Gauze is then packed between the ribs and the underlying periosteum and pleura and also into the remainder of the wound. This constitutes the first stage.

One or more days later, the length of the interval depending upon the nature of the case, the second stage is performed. The packing is removed and the bare ribs are resected. The correctness of the location is then verified by aspiration with a needle and the abscess is opened with the cautery (actual or diathermy) in its most superficial aspect. Enough of the roof of the abscess is then removed with the cautery to allow wide open packing of its cavity. In case the abscess is unusually large, it may be necessary occasionally to remove a segment of one of the adjacent ribs to allow a sufficiently wide opening. The cavity and wound are then packed with dry gauze. No sutures are taken in the wound. This wide exposure of the cavity allows a satisfactory inspection of its interior each time the packing is changed during the next few weeks and if, as often happens, a neighboring subsidiary cavity becomes apparent (as suggested by persistence of fever, cough, and sputum), it is immediately sought for and opened through the wound. Such a secondary procedure done early in the convalescence is considered a part of the primary drainage operation. It has nothing to do with the operation of re-drainage referred to later under the discussion of the treatment of unsuccessful cases.

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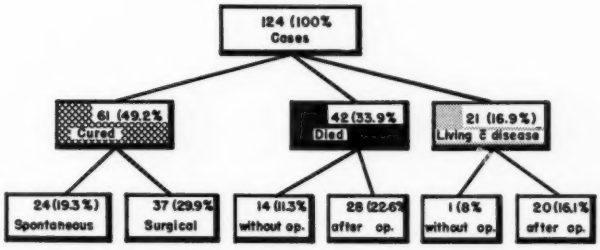


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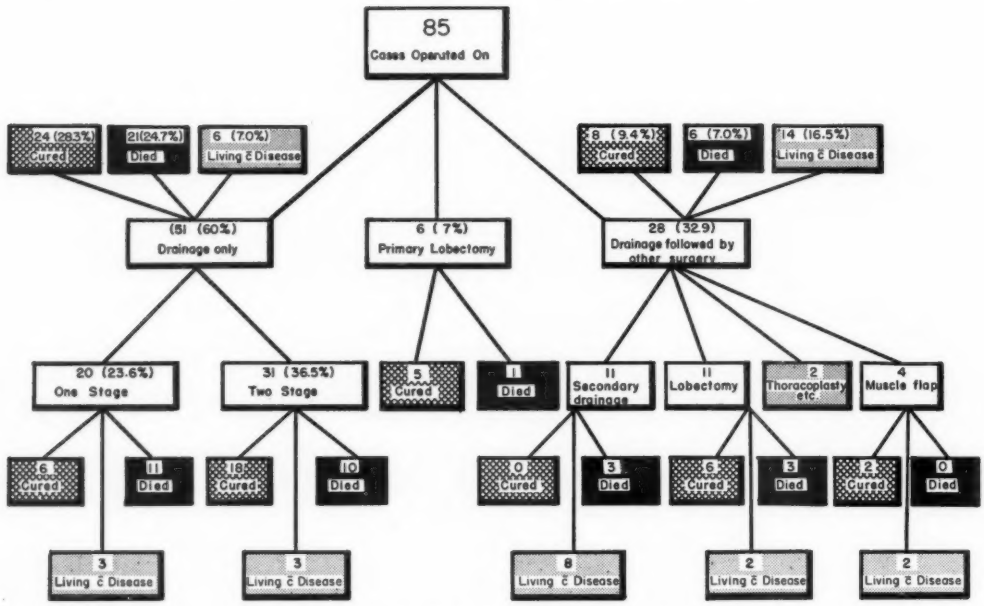


Chart 8. Results in 85 patients operated on.

(6 in this series). Of these, 5 were cured and 1 died. All of the 79 remaining cases were treated first by drainage. A brief reference to Chart 9 shows that simple drainage unaided by any supplementary treatment accounted for only 24, or 30.4 per cent, cures. Twenty-one, or 26.6 per cent, died and 34, or 43 per cent, were not cured by drainage alone. These results are disappointing but undoubtedly bear a relation to the stage of the disease when the operation was carried out and to the severity of the infection.

*Operative mortality.* It has usually been customary to assume that all the deaths which occurred after an operation had been performed represent the operative mortality. In lung abscess this is not so. As has been pointed out, the virulence of the disease is often intense and many patients die early of the disease whether they are operated upon or not. By a careful analysis of the causes of death in all 21 cases ending fatally after drainage (Table III) it is apparent immediately that the majority of those patients died of the disease. There were 6 deaths, however, which in fairness should be ascribed to the effect of the operation. In Cases 7, 13, 18, and 19 (Table III) the fatal outcome was probably because of the wrong choice of operation or a technical error (Case 13). In Case 2 the avertin anesthesia was probably a contributing factor; in Case 11 death was apparently caused by a pulmonary embolus, a common cause of postoperative death.

Granting that these 6 cases represent the total fatalities resulting from operation *per se*, the operative mortality is 7.4 per cent for the entire group of 79 cases after primary drainage. By referring again to Table III one will see that the causes of death in the 15 remaining cases were: spread of infection in the lungs, 7 cases; brain abscess, 5 cases; Streptococcus bacteremia, 2 cases; massive hemorrhage, 1 case. In none of these cases after careful study can the operation fairly be blamed for the result.

*One stage versus two stage drainage.* Reference to Chart 8 shows that of the 51 cases treated by simple drainage only 20 were done in one stage and 31 by the two stage method.

TABLE III.—DEATHS AFTER SIMPLE DRAINAGE

| Case no. | Cause of death | Days after operation | Duration of disease | Extent | Autopsy |
|---|---|---|---|---|---|
| 1 | Brain abscess | 16 | 12 mos. | Entire left lung | o |
| 2 | Fulminating pneumonitis, aspiration of secretions | 2 | 15 mos. | Rt. upper and rt. middle lobes | o |
| 3 | Spread to opposite lung, septic infarct of kidney | 26 | 5 mos. | Large | o |
| 4 | Pulmonary gangrene and spreading bronchopneumonia | 14 | 1 mo. | Large | + |
| 5 | Streptococcus bacteremia | 13 | 6 mos. | Multilocular | + |
| 6 | Brain abscess | 56 | 8 mos. | | + |
| 7 | Spreading pneumonitis (before second stage) | 3 | 12 mos. | Entire lobe | + |
| 8 | Spread to opposite lung with empyema (unrecognized) | 17 | 13 mos. | Multiple | + |
| 9 | Massive hemorrhage | 24 | 7 mos. | Multiple | o |
| 10 | Brain abscess | 28 | 14 mos. | Multiple | o |
| 11 | Sudden embolism, ? pulmonary | 6 | 4 wks. | Large | o |
| 12 | Brain abscess | 16 | 4 mos. | Large | o |
| 13 | Pneumothorax, result of one stage operation | 11 | 5 wks. | Large | o |
| 14 | Amyloid disease. Abscesses in adjacent lung; empyema | 4 | 4 mos. | 2 large | + |
| 15 | One stage operation. Cyanosis ? Spread of infection | 5 | 3½ yrs. | Large multiple | + |
| 16 | Streptococcus bacteremia, ? spreading sepsis in lung | 22 | 5 wks. | Large | o |
| 17 | Acute mediastinitis. Bronchopneumonia | 7 | 2 mos. | Large multiple | + |
| 18 | Bronchopneumonia; spread (before second stage) | 2 | 1½ mos. | Multiple | + |
| 19 | Trochar thoracotomy (wrong operation) | X | 1½ mos. | | + |
| 20 | Spreading infection | 2 yrs. later | 2 yrs. | Large | o |
| 21 | Brain abscess | 7 mos. later | 10 mos. | Large | o |

It appears also that the relative number of cures was greater and the number of deaths smaller in the two stage than in the one stage group. This is probably not significant, however, because many of the one stage cases were so severe that immediate drainage was desired so as to avoid any delay. In those that were less fulminating the two stage operation was usually employed.

Our ideas have changed during the past few years. At first we feared entering the pleural cavity in the performance of a one stage operation and this accident occurred in 1 case in this group. Likewise, we used to allow 7 to 12 days or more for the interval between stages. Several patients died, however, of a rapid spread of the infection before the second stage was done. At present our tendency is to use the two stage operation not only because of the danger of entering the pleural cavity but also to avoid the contamination of the freshly divided tissues of the chest wall. But 24 to 48 hours of contact with a gauze pack is enough to wall off these tissues and the second stage may then be done and the abscess drained much more promptly than formerly. Our recent experience has shown that with accurate localization of the abscess one can find the region where the pleura is adherent, although in many cases the area is small and gauze packing will insure a wider safe space in which to enter the abscess. Our experience confirms the contention of Neuhof that all lung abscesses are peripheral with reference to the lung.

*Cases in which secondary operations were performed.* An interesting and important problem is presented by those cases in which simple drainage is unsuccessful. Chart 10

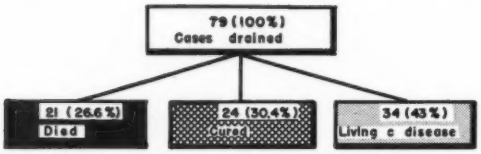


Chart 9. Results after drainage alone.

gives a summary of the treatment and results in the 34 cases of patients left uncured after drainage alone. Six of these were not operated upon again, but are still not cured. Twenty-eight patients were operated upon one or more times after the failure of primary drainage.

Four types of operation were used; in some cases two or more types were used on the same patient. Eleven were subjected to *secondary drainage* operations. The significant fact about this group is that none was healed by secondary drainage, in some cases repeated several times. Three died and 8 were left with disease. *Lobectomy*, performed in this group 11 times, resulted in 6 cures, 3 deaths, and left 2 still with disease. *Thoracoplasty* was abandoned early as unsuitable, but in the 2 cases in which it was used, it was unsuccessful. A *muscle flap operation* was used in 4 cases. In 2 of these a recurrence developed. In one of the latter this occurred 2 years after the abscess cavity was believed to have been closed successfully.

TABLE IV.—COMPARISON OF RESULTS IN EACH GROUP

| | 1924–1932 Per cent | 1933–1937 Per cent |
|---|---|---|
| Cured | 34.8 | 49.2 |
| Died | 37.1 | 33.9 |
| Alive with disease | 28.0 | 16.9 |
| Cured spontaneously | 21.4 | 19.3 |
| Cured by surgery | 12.8 | 29.9 |
| Operative mortality (drainage cases) | 12.5 | 7.4 |
| Number of patients operated upon | 45.7 | 68.5 |

To summarize the results in this group of cases of secondary operation: In spite of every effort only 8, or 28.5 per cent, were cured; 6, or 21.4 per cent, died, and 14, or 50 per cent, remained uncured.

*Results of surgical treatment by all methods —primary and secondary.* The results of the surgical treatment of lung abscess in this series are on the whole rather disappointing. Of the 85 patients operated upon by all methods, 37, or 43.5 per cent, are cured; 28, or 32.9 per cent, died; and 20, or 23.6 per cent, are alive with disease. These

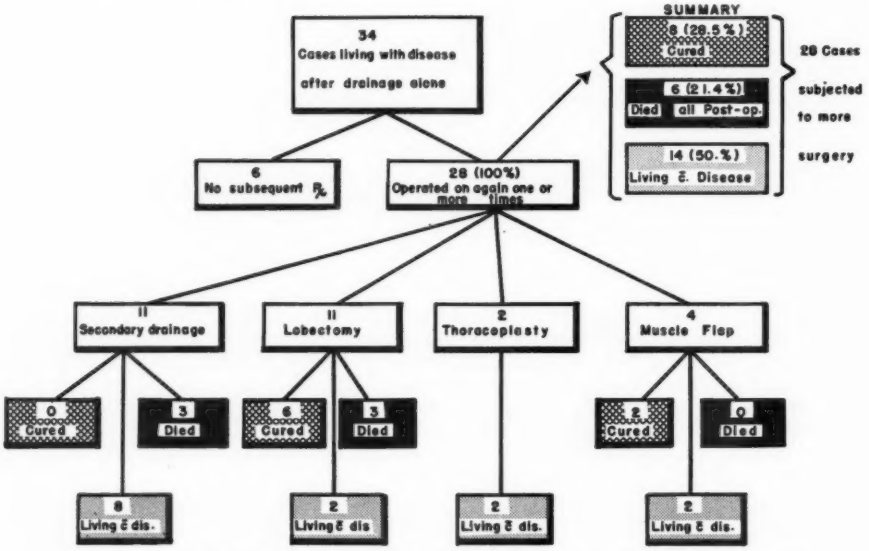


Chart 10. Results of further surgery in patients living with disease after drainage alone.

statistics are better, however, than those of the last report from this clinic (King and Lord) which are based upon 96 patients operated upon. Of these 27, or 28.1 per cent, were cured; 38, or 39.5 per cent, died; and 31, or 32.3 per cent, remained alive with disease. This comparison is interesting. One notes a significant improvement in mortality, but as was pointed out before, the majority of operative deaths are due to the disease and are not attributable to the operation. It should be pointed out here, however, that the previous series was not carefully analyzed with this point in mind. The method of drainage used then was usually a one stage operation through a small incision, often with rather incomplete localization of the process, and insertion of a rubber tube or cigarette wick drain without any unroofing of the cavity as practiced now. As a result, it is quite possible that more of the deaths were definitely due to the operation. The actual operative mortality was estimated at that time to be in the neighborhood of 12.5 per cent (King and Lord). As described here, the operations used in the present series tended to be more radical and on the whole gave more complete drainage. The significant difference, however, is the marked improvement in the number of cures (from 28.1 to 43.5 per cent). This, we believe, is because in the present series the results of both primary lobectomy (5 cures) and secondary lobectomy (6 cures) come into play and were not a factor in the former group, and also because of the improvement in the technique of the drainage operation with more radical unroofing of the cavity.

In conclusion, a comparison of the results in each group is of interest (Table IV).

Here again one is forced to conclude that the improvement in results is because of the increased number of patients operated upon and the increased use of more radical measures including lobectomy in properly selected cases. One should note, however, that the percentage of spontaneous cures has remained essentially the same. Sufficient data are not available in reference to the earlier series to determine whether a more prompt resort to surgery was a factor in this improvement, but there was probably very little difference.

## CONCLUSIONS

By this study certain facts which may be used further to improve our results in this serious disease seem apparent. It is suggested that they be utilized with this in mind, and the following suggestions are offered:

1. Patients should not be allowed to go without operation longer than 4 months from the onset of disease.

2. Patients with abscesses which do not show definite regression should be operated upon early—within 6 to 8 weeks after onset; often as soon as they are seen and the diagnosis confirmed.

3. The interval between stages of the two stage operation should in general not exceed 4 to 5 days; in the desperately sick patients, not more than 24 to 48 hours.

4. Certain cases, notably the upper lobe abscesses which are not too acute, should be subjected to primary lobectomy in preference to drainage.

5. Certain cases should be drained as a preliminary procedure with the idea of performing a lobectomy at a later time.

6. The operation of re-drainage should be abandoned. Patients who remain unhealed after primary drainage will do better if treated by lobectomy. (Note: The opening of secondary cavities not reached at first operation is not classified as re-drainage.)

7. All patients with lung abscess should have the benefit of the combined judgment of the internist, the bronchoscopist, the thoracic surgeon, and the roentgenologist, if the best results are to be obtained.

Given ideal conditions for the proper study and treatment of these patients, much better results can now be obtained than formerly but there still remains a large group of patients who will die of the disease. If further improvements are to be made in our results, they will probably emerge from a better understanding of the bacteriology and the related problems of immunology in these cases.

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# ACUTE CHOLECYSTITIS

## A Review of 320 Cases

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IT is not surprising that the treatment of acute cholecystitis lends itself to so much controversy and difference of opinion, for it is a condition, the recognition of which depends primarily on that most inexact of sciences—clinical impression. The diagnosis of acute cholecystitis has to be made without the aid of the newer diagnostic methods which are so useful in the recognition of chronic cholecystitis. Thus, in the final analysis, the management of a case must rest on the clinical judgment of the observer, a factor obviously subject to great variation.

In an endeavor, therefore, to establish certain basic facts, we have reviewed 320 of our own cases of acute cholecystitis which we present herewith. In general we have followed the practice of early operation introduced by the senior author (R. D. Mc.) over 20 years ago, but the individual surgeon has been guided by his own surgical judgment. Only one arbitrary rule has been followed and that is the necessity for considering immediate operation when the relative proportion of polymorphonuclear leucocytes approaches 90 per cent or the total leucocyte count rises above 20,000 per cubic millimeter.

The selection of cases for study presented a problem, for in reviewing our records we soon found that there were three types of acute cholecystitis—clinical, surgical, and pathological. The first two diagnoses are based on impression only, while the pathological diagnosis is based on facts. Therefore, the cases falling into the first two groups were discarded, and only those cases on which a pathological diagnosis of acute cholecystitis had been made were studied.

The criterion for diagnosis of acute cholecystitis as established in our pathological department by Dr. Frank Hartman is microscopical evidence of polymorphonuclear infiltration of the gall-bladder wall. This excluded from our review many cases in which diagnosis of acute cholecystitis had been made by both the clinician and the operating surgeon. However, because the results of immediate operation in this special group are so uniformly good, we were of the opinion, rightly or wrongly, that their inclusion in a statistical study of acute cholecystitis was not justified because they were not truly examples of the condition. If these cases of simple edema of the gall bladder which accompanies gall stone colic had been included, our results would have been materially affected, and a brief for, rather than against, immediate operation would have been presented.

*Sex.* Acute cholecystitis, like chronic cholecystitis, is more common in the female than in the male, in the proportion of 2:1, a figure that is almost the exact reverse of the ratio obtained in our cases of acute appendicitis (7). Men, however, seem to be more prone to acute cholecystitis than women, for males comprise 30 per cent of our cases of acute cholecystitis as contrasted with 20 per cent of our cases of chronic cholecystitis.

*Age.* Acute cholecystitis is a disease of middle life, for 76 per cent of our patients were between the ages of 30 and 59. This again is in contrast to our statistics for acute appendicitis which showed that only 50 per cent of our patients were over 30 years of age (7). The age of the patients had a very definite bearing on mortality, for of the 108 patients under 40 years of age, there was only 1 death —a mortality rate of 0.9 per cent, while in the group of 48 patients over 60 years of age there were 5 deaths, a mortality rate of 10.5 per cent. In the middle aged group of 164 patients between the ages of 40 and 60, there were 11

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deaths, a mortality rate of 6.7 per cent This shows very clearly that the death rate from cholecystectomy for acute cholecystitis rises with each succeeding decade.

*Obesity.* The overweight patients of this series numbered 163, or 50.9 per cent. Obesity in itself apparently had very little effect on the mortality, for of the 17 deaths, only 9, or 52.9 per cent, were overweight.

### PRE-OPERATIVE HISTORY

Forty, or 12.5 per cent, of the patients had no previous warnings of gall-bladder disease. The others had suffered one or more attacks, usually over a period of years.

Two hundred and seventy-eight, or 86.8 per cent, patients had been treated medically and 9, or 2.8 per cent, had undergone cholecystostomy.

Nausea and vomiting were the most constant symptoms of acute cholecystitis, appearing in 91.2 per cent and 83.4 per cent, respectively, of the cases. Clinical jaundice was present in one-fourth of the patients and one-fifth of them complained of chills at the onset of the disease. Pruritus was a distressing symptom in 2.2 per cent of the cases, and further evidence of interference with biliary function was shown by the finding of highly colored urine in 12.8 per cent and of clay-colored stools in 8.7 per cent of the patients.

Pain and tenderness was present in either the right upper quadrant or the epigastrium in 90 per cent of the patients. A mass was palpated in one-fifth of the examinations. Most of these masses were found to be due to greatly distended gall bladders, but in some instances the mass represented the gall bladder surrounded by protecting adhesions and in others it was evident that the examiners had palpated the projecting edge of the liver. Muscle spasm of varying degree was observed in 88.1 per cent but the degree of spasm was not a gauge of the severity of the infection.

The group of patients whose maximum pre-operative temperature was above 102 degrees F. showed a mortality rate of two and one-half times the mean death rate for the series. This observation may be of some prognostic value, for it was the only pre-operative finding that indicated in any manner the group of cases in which there was a high operative mortality. This group, of course, represents the more seriously ill patients in whom the mortality might be expected to be higher, but the inference still remains that these patients should have careful, extended observation and preparation for the operation.

Roentgenological confirmation of the diagnosis was sought in 155 cases, 48.4 per cent, and positive findings resulted in 116, or 74.8 per cent, of these examinations. The positive results in three-fourths of the cases make the procedure well worth while, and it is withheld only in the very ill patients or those in whom a considerable degree of liver insufficiency is suspected.

Pulmonary complications increased the operative risk three times and cardiac complications doubled the risk.

In this series the cases have been divided into three groups depending upon the duration of symptoms prior to operation. Group I, designated as the "emergency group" includes those operated upon within 24 hours after onset of symptoms; group II, the "early group," includes those operated upon between 24 and 72 hours after onset; and group III, the "delayed group," those operated upon after the lapse of 3 or more days from onset. The divisions are a modification of the groupings used by Cave in his recent discussion of acute cholecystitis.

Study of Table I shows little difference in the percentage of deaths of groups I and II but comparison of groups I and II with III suggests that the optimum time of operation is after the third day of the onset of symptoms. The low rate of 3.4 per cent in group III compared with the rates of 8.3 per cent and 7.3 per cent in the earlier groups is due to the subsidence of the infection, the response of the body defenses, and the more thorough preparation of the patient for surgery.

The length of *pre-operative hospitalization* for observation and preparation is covered in Table II. This table is also divided into groups having 24 hours, 24 to 72 hours inclusive, or more than 72 hours of hospitalization. There is a favorable difference between the emergency group which, with less than 24 hours of preparation, had a mortality of 8.4 per cent

TABLE I.—DURATION OF ILLNESS AT TIME OF OPERATION

| Groups | No. of patients | Percentage | No. of deaths | Percentage |
|---|---|---|---|---|
| 0 to 24 hours— | | | | |
| Emergency..... | 48 | 15.0 | 4 | 8.4 |
| 24 to 72 hours—Early, | 96 | 30.0 | 7 | 7.3 |
| More than 72 hours— | | | | |
| Delayed..... | 176 | 55.0 | 6 | 3.4 |
| Totals..... | 320 | 100.0 | 17 | 5.3 |

and the early and delayed groups which had 1 or more days' hospitalization prior to operation. Comparison of group III with I and II reveals a rate of 3.1 per cent contrasted with rates of 5.2 per cent and 8.4 per cent. Again the implication appears that a delay until more than 3 days after onset and hospitalization reduced the hazard of operation; however, the figures do not compare the degrees of sickness of the patients. It must be acknowledged that the more seriously ill patients had surgical treatment early; that is, as soon as they could be fortified against the shock of the operation by rest, sedation, and fluids. Since more of the very ill patients had cholecystectomy before 3 days of hospitalization than after 3 or more days of preparation, the moderately higher death rate in groups I and II is partly explained. It must be conceded, however, that hospitalization for observation and preparation is a valuable procedure and that the emergency operation is the most dangerous.

*Pre-operative diagnosis.* The diagnosis of cholecystitis was made prior to operation in 96.3 per cent of the cases. The greater number of these were thought to be acute, but in a few instances the acuteness of inflammation was not recognized before exposure of the gall bladder at operation. Among the diagnostic errors, pancreatitis and perforated ulcer each appeared twice and appendicitis on four occasions.

The difficulty of correlating the clinical surgical and pathological diagnosis is emphasized by noting that in 35 of the 320 cases, or in 10.9 per cent, the operating surgeon made a diagnosis of chronic cholecystitis, while the specimen on pathological examination revealed evidence of acute cholecystitis. No doubt many of these erroneous diagnoses of chronic cholecystitis were made because the

TABLE II.—PRE-OPERATIVE HOSPITALIZATION

| Groups | No. of patients | Percentage | No. of deaths | Percentage |
|---|---|---|---|---|
| Less than 24 hours— | | | | |
| Emergency..... | 71 | 22.2 | 6 | 8.3 |
| 24 to 72 hours—Early. | 154 | 48.0 | 8 | 5.2 |
| More than 72 hours— | | | | |
| Delayed..... | 95 | 29.8 | 3 | 3.2 |
| Totals..... | 320 | 100.0 | 17 | 5.3 |

patient had had a clinical diagnosis of chronic cholecystitis. In general, however, the tendency was to overrate the severity of the condition found at operation. For example, in 66 instances the surgeon recorded a diagnosis of gangrenous gall bladder while the pathologist recognized only 29 cases of gangrene, and similarly there were 40 surgical diagnoses of empyema of the gall bladder, of which only 15 were proved pathologically.

### OPERATIVE PROCEDURES

*Cholecystectomy versus cholecystostomy.* The gall bladder was removed in all of the cases in this series. Cholecystostomy is a rare operation at the Henry Ford Hospital.

*Appendectomy.* The close association of appendicitis and cholecystitis, both acute and chronic, is well recognized and has been frequently commented upon in the literature. The tendency and the teaching in general has been to advise against the removal of the appendix at the same time cholecystectomy is performed for acute cholecystitis. However, in our series, the removal of the appendix did not add to the mortality since 39.0 per cent of the patients had appendectomy performed in addition to removal of their gall bladder with a mortality rate of 2.4 per cent.

*Common duct drainage.* Edema of the structures usually obscures the common duct and makes its identification difficult. The usual teaching therefore is against choledochotomy. However, in the presence of a common duct stone, opening the duct becomes imperative. The mortality rate in our cases was not adversely affected when the common duct was opened and drained.

### ASSOCIATED CONDITIONS

*Gall stones.* Gall stones were present in all but 29, or 9.1 per cent, of the 320 patients. The gall stones were located in the gall bladder in

87.7 per cent of the cases, in the cystic duct alone in 2.5 per cent, and in the common duct alone in 1.2 per cent. Gall stones were found in the common duct 20 times, i.e. in 6.2 per cent of the cases, though it is probable that their presence was sometimes overlooked owing to the difficulty of palpation occasioned by the edema of the structures. The rôle of calculus obturation of the cystic duct in the etiology of acute cholecystitis is emphasized by the finding of gall stones in 71 of the cases of 22.2 per cent of the series.

*Pancreatitis.* The close association of cholecystitis and pancreatitis has long been recognized. In this series, pancreatitis was observed 18 times, or in 5.7 per cent of the cases. The involvement was acute in 2 instances, subacute on one occasion and consisted of thickening of the organ only in the 15 remaining cases. The infrequency of acute involvement of the pancreas in acute cholecystitis as we have commented upon elsewhere (3) suggests that infection plays a minor rôle in acute pancreatitis and appears to substantiate the chemical origin of the disease.

### GALL-BLADDER CULTURES

Bacillus coli appearing in 25.7 per cent of the cultures, headed the list as the commonest organism cultivated. Growth of staphylococci and of streptococci each accounted for 11.5 per cent of the positive culture and Bacillus lactis aerogenes and Bacillus coli mixed with other organisms were obtained in four occasions each. Bacillus typhosus, Bacillus dysenterica, Bacillus influenzæ, and yeast cells each appeared once. Negative culture obtaining in nearly one-half of the gall bladders cultured indicates that obstruction and chemical agents are factors in many cases of acute cholecystitis.

### PATHOLOGICAL DIAGNOSIS

A diagnosis of chronic cholecystitis with acute exacerbation was made on 43.7 per cent of the patients. A previous attack of cholecystitis or long standing gall-bladder disease appears to confer some degree of immunity, for the lowest operative death rate, 3.6 per cent, was found in the group of patients whose acute cholecystitis was superimposed upon pre-existing cholecystic disease. Further evidence on this point is introduced by noting that the death rate in approximately the same number of patients with primary acute cholecystitis was 6.1 per cent or almost double that of the rate of those whose gall bladder had been infected previously.

TABLE III.—MAXIMUM POSTOPERATIVE TEMPERATURE

| Temperature range F. | No. of patients | Percentage | No. of deaths | Percentage |
|---|---|---|---|---|
| 98.8–100.8 | 85 | 26.6 | 0 | 0.0 |
| 101 –102.8 | 185 | 57.8 | 3 | 1.6 |
| 103 –108 | 50 | 15.6 | 14 | 28.0 |
| Totals | 320 | 100.0 | 17 | 5.3 |

Gangrene of the gall bladder was the most serious condition from the standpoint of mortality, for it showed a death rate of 10.4 per cent, almost double the rate of 5.3 per cent given by the series as a whole.

Empyema of the gall bladder occurred in only 5.9 per cent of the cases. There was only 1 death in this group, so that the mortality rate was 5.3 per cent or exactly the same as the mean for the entire series.

### POSTOPERATIVE COURSE AND COMPLICATIONS

The majority of patients had relatively stormy postoperative courses. The difference between the reaction of these patients and of those recovering from cholecystectomy for chronic cholecystitis is striking. A general indication of the postoperative course is given by noting that 67 per cent of the patients required repeated administrations of intravenous glucose to maintain the glycogen content of the liver and 10.6 per cent required blood transfusions.

Some idea of the relatively sharp febrile reaction which occurs following removal of an acutely inflamed gall bladder may be obtained from a consideration of Table III. The cases are divided into three groups. Group I includes the 26.6 per cent of patients whose postoperative reactions were mild as indicated by the postoperative temperature, not rising to 101 degrees F. There were no deaths in this group. Group II is made up of the 57.8 per cent of patients whose postoperative reactions were moderately severe as shown by a temperature range of from 101 degrees F. to 102.8 degrees F. There were 3 deaths in the group, a mortality of 1.6 per cent. Consider-

ing groups I and II together, i.e., those patients whose temperature did not reach 103 degrees F., we find only 3 deaths in 270 patients, a mortality of 1.1 per cent. Group III consisted of the 15.6 per cent of patients whose postoperative reactions were severe, as evidenced by postoperative temperatures which ranged from 103 to 108.8 degrees F. There were 14 deaths in the group of 50 patients giving a mortality rate of 28 per cent.

A fever of 103 degrees F. or over, after an operation for the removal of an acutely inflamed gall bladder indicates a serious condition of the patient, and should be considered as being of grave prognostic significance. All 4 patients whose temperature went to 107 degrees F. or over died. In 2, the cause of death was given as peritonitis and in the 2 others, the fatality was listed as "liver death" (5).

Pulmonary complications, the commonest of postoperative complications in most series of cases presented (6), took second place in our series. A total of 30 patients, or 9.4 per cent of the series, were affected as follows: bronchitis, 9; bronchopneumonia, 6; pulmonary collapse, 5; asthma, 3; lobar pneumonia, 2; infections, 2; lung abscess, 1; and 2 patients had reaction of latent pulmonary tuberculosis. There were 4 deaths, all from pneumonia, a mortality rate of 13.3 per cent.

We desire to stress the value of carbon dioxide inhalations in the immediate postoperative period and the use of the oxygen tent when the respiratory rate rises above 30 per minute in the prevention and treatment of pulmonary complications.

Myocardial weakness was encountered in 15 patients in 4.7 per cent of the series. The diagnosis was myocarditis on 10 occasions; auricular fibrillation, 3 times; and auricular flutter, twice. Two deaths were from myocardial failure, a mortality rate of 13.3 per cent.

Bleeding from the wound or deeper structures was not of common occurrence, being noted in only 11 patients, or 3.5 per cent of the series. Hemorrhage was slight in 8 instances, moderate on 2 occasions, and severe enough to be fatal in 1 patient.

Peritonitis is a relatively infrequent complication of cholecystectomy for acute cholecystitis. It was seen in only 2.2 per cent of our cases, and of the 7 examples, 2 died, giving a mortality rate of 28.6 per cent. The ability of the peritoneum to handle the gall-bladder contents is emphasized by noting that there were only 2 deaths in the 22 patients in whom the gall bladder perforated before operation, and in 1 of these, the cause of death was given as myocarditis. This gives a mortality rate of 9.1 per cent in perforation of the gall bladder with subsequent operation. The peritoneal fluid was cultured at operation in only 18 instances, of which 5, or 27.8 per cent, were negative. Positive cultures for staphylococcus were obtained on 5 occasions; Bacillus coli on 4; streptococcus on 3; and Bacillus typhosus on 1.

Phlebitis, a disabling, though not dangerous complication, was noted 6 times, or in 1.9 per cent, of the patients. There were no deaths. In the prevention of this complication, we follow the teaching of Poole and insist upon our patients exercising in bed. Early and repeated movements of the arms and legs plus deep breathing and frequent changing of position improves the circulation in the iliac veins and must be a definite factor in lowering the incidence of thrombus formation.

Wound separation, a serious postoperative complication, occurred 4 times, or in 1.3 per cent of our cases. There was 1 death following an ill advised attempt at secondary suture of the wound, carried out before a study of our records impressed upon us the hazard of such a procedure (2).

Because of the proximity of the gall bladder to the subphrenic space, and because of the frequency of extension of inflammation outside the gall bladder wall, one might expect a subphrenic abscess to be of frequent occurrence. However, it was found in only 1 of our cases, and the patient recovered after surgical drainage.

Pulmonary embolism, the most fatal of all complications, appeared twice and showed a 100.0 per cent mortality. This complication often considered as a pulmonary complication rightfully belongs with "phlebitis," but since it is a preclinical phlebitis the conditions are described separately. The recent work on heparin (8) is interesting in this connection.

It may be that the absorption of liver products resulting from incidental damage to the liver parenchyma during cholecystectomy for acute cholecystitis may be a factor in preventing the more frequent occurrence of this dangerous complication.

The usual period of hospitalization after operation for chronic cholecystitis at the Henry Ford Hospital is 17 days and yet only 14.2 per cent of patients were able to leave the hospital on the seventeenth postoperative day after cholecystectomy for acute cholecystitis. Furthermore, only 45.9 per cent of the patients were discharged from the hospital by the twenty-first postoperative day, and 20.9 per cent had their hospital stay prolonged beyond thirty days.

## MORTALITY

There were 17 deaths in the 320 patients subjected to cholecystectomy for acute cholecystitis, or a mortality rate of 5.3 per cent. The deaths resulting from cardiac and pulmonary complications, peritonitis, hemorrhage, and shock, have already been considered. Three of the fatalities occurred from overlooking other pathological conditions present which, at the time of operation were unrecognized, and were revealed only at postmortem examination. In 1 case an appendix abscess was the focal point of a fatal pyelophlebitis and in 2 cases concomitant perforated ulcer was responsible for the fatal issue. In all 3 patients the gall bladder showed definite evidence of acute inflammation and was accepted by the surgeon as being responsible for the clinical course prior to operation. This association of acute cholecystitis and perforated peptic ulcer we have found in 2 other cases, both of which recovered after the ulcer was dealt with. In one the condition was recognized at operation and in the other, operation was performed 3 days after cholecystectomy.

Two of the 17 deaths occurred in patients whose postoperative clinical course were characterized by hyperpyrexia, coma, and death. The cause of death in these cases was considered to be due to hepatic insufficiency on the so-called "liver death" of Heyd.

Fatal cases do not long survive the operative interference, for 82.3 per cent of the 17 deaths had taken place by the fifth postoperative day. This finding suggests that liver insufficiency may be a factor in many of the fatal cases as well as those definitely attributed to "liver death."

## FOLLOW-UP

The length of time most of the patients were under observation following discharge from the hospital is inadequate for establishing any data of definite statistical value for only 50.3 per cent of the patients were followed over 6 months. Five deaths occurred during the period of observation, 2 from pulmonary tuberculosis alleged to have been activated by the operation, 1 from myocarditis, 1 from lung abscess and 1 from carcinoma of the head of the pancreas.

A total of 42 patients, or 15.1 per cent of the 278 patients who were observed, returned for treatment. Of these, one half complained of the same symptoms as were present before operation. All were relieved by medical treatment. A total of 19 patients, or 45.2 per cent of those who returned, had symptoms suggestive of common duct stone. Of these, 14 had relief of symptoms from medical measures, and 5 were subjected to choledochotomy: stones were removed in 3 instances, and on 2 occasions, the common duct exploration was unfruitful but the patient improved after T-tube drainage. Two patients were operated upon for common duct stricture with satisfactory results, but the surgeon may have been over-optimistic in not attributing the condition to operative traumas.

## SUMMARY

1. The mortality in 320 consecutive operations for acute cholecystitis which were performed at the Henry Ford Hospital was 5.3 per cent.

2. The maximum pre-operative temperature is of some prognostic value for the death rate on patients whose pre-operative temperature was above 102 degrees F. was three times that of those whose temperature remained below 102 degrees F.

3. Pre-operative pulmonary disease increased the risk of operation three times, and cardiac disease doubled the operative risk.

4. The lowest mortality rate was obtained in patients whose operation was delayed for at least 72 hours from the symptoms.

5. The highest mortality rate obtained in the gangrenous cases.

6. Gall stones were present in 90.9 per cent of the cases.

7. A postoperative temperature of above 103 degrees F. indicates a serious condition of the patient and is of considerable prognostic value for the mortality among the group of patients whose postoperative temperature rose above 103 degrees F. was 28 per cent.

8. The seriousness of acute cholecystitis is emphasized by the fact that less than 15 per cent of patients were discharged by the seventeenth postoperative day and over 20 per cent remained in the hospital longer than 30 days.

9. The short duration of life in the fatal cases, over 80 per cent of the deaths occurred before the fifth postoperative day, suggests that hepatic insufficiency might be a factor in the mortality.

## CONCLUSIONS

Removal of the gall bladder during an attack of acute cholecystitis gives good results and the mortality is within reasonable limits. From this study of our cases, we are forced to the conclusion that the best results in acute cholecystitis are obtained by deferring operation until at least 72 hours have elapsed since the onset of the disease. These results will be further enhanced by an adequate period of pre-operative hospitalization. Our results improved with each succeeding 24 hours of preparation, reaching their maximum after 72 hours.

It is probable that immediate or early operation can be practiced with a low mortality in approximately 85 per cent of patients with acute cholecystitis, but in the remaining 15 per cent the mortality rate will be prohibitively high. At the present time there is no known method of recognizing the latter group other than by clinical judgment. Therefore, until the time arrives when these patients can be diagnosed and excluded, it would appear better to delay operation in the whole group until the fluid balance is restored, the glycogen content of the liver is augmented, and an estimate of liver function is made. Cases of impending gangrene or perforation must be of course treated as any other surgical emergency.

We believe further that the value of liver function tests has not been appreciated fully, and we are inclined to agree with Ivy that surgery should not be attempted on the biliary tract without the benefit of these tests. In acute cholecystitis it is probable that the routine use of those liver function tests, which are not harmful, will lower the mortality rate by recognizing liver insufficiency and preventing untimely operations.

The authors wish to express their appreciation of the assistance given by Dr. Edward Canipelli in the compilation of this material.

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# SCOLIOSIS

## Its Experimental Production and Growth Correction; Growth and Fusion of Vertebral Bodies

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BY implication as well as fact, the term idiopathic scoliosis designates that group of structural, rotary, lateral curvatures of the spine of unknown or unestablished etiology. Upon the basis of the experimental data which follow and some pertinent clinical evidence to be discussed, it is proposed that inequality of growth on the 2 sides of vertebral bodies of a portion of the spine or, in other words, unilateral growth disturbances are either totally responsible or at least contributory in a large measure to the development and progression of this group of curvatures.

Two possible clinical applications of these experimental data are also proposed. These are (1) unilateral operative arrestment of growth of several vertebral bodies for purposes of gaining some correction of curvatures during the subsequent period of growth, and (2) the accomplishment of vertebral fixation by fusing vertebral bodies directly.

### EXPERIMENTAL DATA

Kid goats were used for these studies because they are particularly rugged. Compared to other newborn animals they are remarkably tolerant of major surgical trauma and seldom acquire disease.

All kids were less than 4 weeks old when operated upon. The bodies of the lumbar vertebræ were approached retroperitoneally through an incision parallel to the lateral border of the erector spinæ muscles from the twelfth rib to the level of the crest of the ilium and thence directed anteriorly for a short distance. The bodies were easily exposed by retracting the perireneal fat, kidney, and psoas muscle mesially and anteriorly. The lumbar vessels which pass laterally at the center of the bodies were divided between ligatures and the common ligaments and periosteum split longitudinally, elevated, and retracted to expose the bone and epiphyseal cartilages.

The bodies of the dorsal vertebræ were approached extrapleurally through an incision which paralleled the lateral border of the erector spinæ muscles from the ninth to the eleventh ribs and then followed the eleventh rib anteriorly to the posterior axillary line. The eleventh rib was resected from its neck to the posterior axillary line. Through the bed of this rib the endothoracic space was entered, and the parietal pleura was carefully separated from the thoracic wall and retracted anteriorly and mesially until the anterior surface of the vertebral bodies had been exposed. The intercostal vessels, which like the lumbar vessels course laterally over the surface of the bodies, were divided between ligatures. The exposure was completed by dividing the common ligaments and periosteum longitudinally and then retracting them.

With the vertebral bodies thus exposed either above or below the diaphragm, various operative procedures were carried out. In several animals both lumbar and thoracic vertebræ were operated upon but always in 2 stages.

The animals were killed 10 months later when they were 11 months of age, and the spines were removed for comparative studies.

*1. Growth of vertebral bodies.* Regarding the source of growth of vertebral bodies there exists much disagreement. There is the question of interstitial, longitudinal growth, and among those who believe that there is no interstitial growth, there is disagreement as regards the proportion of length gained from the epiphyseal cartilages at the 2 ends.

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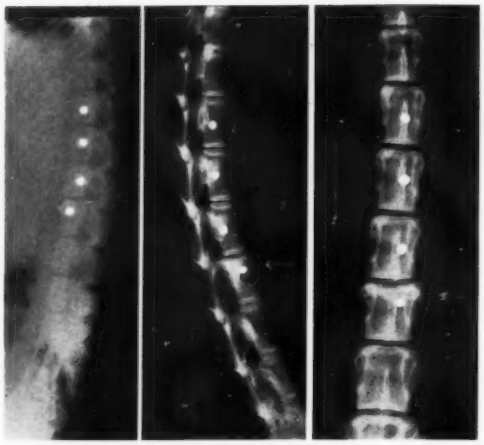

Fig. 1. Goat 11, Table I. Shot markers in the bodies of first, second, third, and fourth lumbar vertebræ, showing longitudinal growth during a period of 10 months. The roentgenogram at the left was made immediately following operation when the goat was 3 weeks of age; the 2 to the right 10 months later. Note that the shots in the 3 proximal vertebræ have retained their original positions equidistant from the ends. Growth was arrested from the proximal end of the distal fourth lumbar vertebra, and as a result note failure of this end of the vertebra to move away from the shot, in other words, failure of growth. The resultant shortening of this vertebra and the absence of its proximal growth cartilage are apparent in both anteroposterior and lateral views.

As shown by the data which follow, the vertebral bodies of goats gain length solely from the epiphyseal cartilages and the increments from both ends are equal.

In each of 4 kids approximately 2 weeks of age, holes were drilled in several vertebral bodies midway between the ends and steel shots placed in the drill holes. Roentgenographic records were made both immediately following operation and 10 months later. At operation and at postmortem examination 10 months later direct measurements were made of the distances from each shot to the intervertebral discs immediately proximal and distal to it and of the distance between the shots themselves. These comparative measurements are listed in Table I.

In 2 goats the shots were placed in 4 contiguous vertebræ at their centers. The roentgenographic records of these animals are illustrated in Figures 1 and 2. It will be observed from both roentgenographic and

TABLE I.—DISTANCE FROM SHOT MARKER TO ENDS OF VERTEBRAL BODIES RECORDED IN MILLIMETERS[1]

| | L. 1 | | L. 2 | | L. 3 | | L. 4 | |
|---|---|---|---|---|---|---|---|---|
| | P. | D. | P. | D. | P. | D. | P. | D. |
| Goat 11—Age: | | | | | | | | |
| 1 month | 8 | 7 | 8 | 8 | 8 | 8 | 7* | 8 |
| 10 months | 14 | 12 | 13.5 | 14 | 14 | 14 | 8* | 15 |
| Goat 15—Age: | | | | | | | | |
| 1 month | 8.5 | 8 | 8.5 | 9 | 8.5 | 9 | 8* | 9.5* |
| 10 months | 13 | 12.5 | 14 | 15 | 14.5 | 15 | 9* | 11* |
| Goat 3—Age: | | | | | | | | |
| 1 month | .... | .... | .... | .... | 9* | 8 | 6 | 10 |
| 10 months | .... | .... | .... | .... | 10* | 13 | 13 | 15 |
| | | | | | 6† | | | |
| | | | | | 6.5† | | | |
| Goat 4—Age: | | | | | | | | |
| 1 month | .... | .... | .... | .... | 8* | 8 | 8 | 9 |
| 10 months | .... | .... | .... | .... | 9* | 14 | 14.5 | 15 |
| | | | | | 5† | | | |
| | | | | | 5† | | | |

[1]The ends are indicated as P, proximal; D, distal; the vertebræ are L, or the first, second, third, and fourth lumbar.
*Growth arrested surgically.
†Distance between shots in diaphysis and epiphysis.

actual measurements that the shots in the 3 proximal vertebræ retained their same relative positions in respect to the ends of the vertebral bodies. In other words, the increments from the 2 ends were equal.

In the distal vertebra of each kid growth was arrested on the side operated upon in addition to placement of shot markers. Growth was arrested from only the proximal end in one and from both ends in the other. This arrestment of growth was accomplished by removing as much of the presenting epiphyseal or growth cartilage as possible. In the first animal no length was gained from the proximal or arrested end, whereas a normal gain in length took place from the distal or undisturbed epiphyseal cartilage (Fig. 1). In the second animal there was no growth in length from either end on the side operated upon; the original length of the body on that side was maintained (Fig. 2) (Table I, goats 11 and 15).

Somewhat more graphic confirmatory evidence that longitudinal growth is acquired from the epiphyseal cartilages only was supplied by observations in 2 additional goats. In each, shots were placed in the bodies of 2 contiguous vertebræ and growth was arrested from the proximal end of the proximal one of these 2 marked vertebræ. A shot was then firmly wedged into the groove from which the cartilage had been removed and a second shot

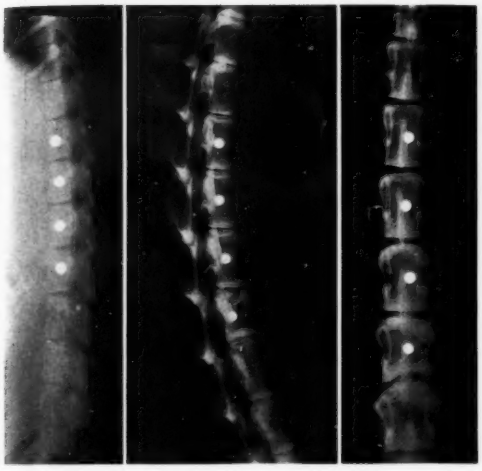

Fig. 2. Goat 15, Table I. Same as in Figure 1, except that growth was arrested surgically from both distal and proximal ends of the distal fourth lumbar vertebra. Note absence of growth cartilage at both ends and failure of growth as evidenced by shortening. Compare length with adjoining vertebræ.

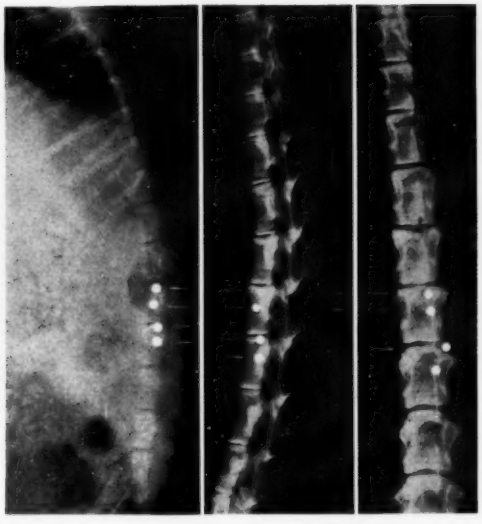

Fig. 3. Goat 3, Table I. In addition to marking bodies of third and fourth lumbar vertebræ with shot, growth was arrested surgically from the proximal end of the third lumbar vertebra and shot markers placed in the proximal epiphysis of this vertebra and in the intervertebral disc between the 2 vertebræ. Note that during a growth period of 10 months, from 1 month old at the left to 11 months at the right, the distance between the upper 2 shots has remained relatively unchanged, showing failure of growth as a result of the operative arrestment. Also note absence of this epiphyseal cartilage. Growth took place from the distal end of this third lumbar vertebra as shown by the increase in the distance between the middle 2 shots. Likewise, the increase in the distance between the lower 2 shots demonstrates the gain in length from the proximal end of the fourth lumbar vertebra.

was placed in the intervertebral disc between the 2 marked vertebræ. In the proximal vertebra, as shown in Figure 3, the distance between the shot in the diaphysis and that in the epiphysis remained relatively unaltered during the 10 months' period of growth. Thus no growth was acquired from the end from which the growth cartilage had been removed. In contrast, the distance between the shot in the diaphysis and that in the intervertebral disc increased considerably. This evidence of growth was also observed in the distal vertebra. The actual measurements are recorded in Table I, goats 3 and 4. It will be noted that in each animal the total growth of the proximal vertebra was distinctly less than that of the distal vertebra.

2. *Experimental scoliosis.* In a series of 6 kid goats, segments of both distal and proximal growth cartilages were removed from one side of 2 or more vertebral bodies, 2 in 3, and of 3 in 3 animals. The cartilages were removed from those halves of the bodies exposed at operation. There resulted arrestment of growth on the side operated upon with continuance of growth on the opposite or undisturbed side. The vertebral bodies became wedge-shaped and distorted the spine into lateral deviation with the concavity of the curvature on the side where growth had been arrested. The lateral bending was accompanied by rotation. The curvatures in 2 goats are illustrated in the photographs and roentgenograms in Figures 4 and 5.

In 3 animals of this series an additional study was made. In addition to growth arrest fusion between contiguous vertebral bodies at another level of the spine was accomplished by placing grafts in contact with the exposed cancellous bone of these bodies. The grafts were laid along one side only, immediately anterior to the transverse processes and were so placed that they bridged the intervertebral discs and established bony continuity between the bodies. In 2 of the animals 4 contiguous

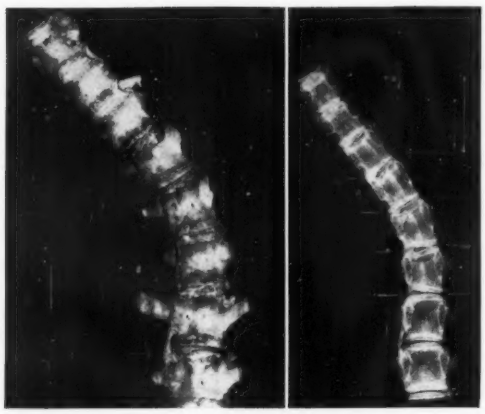

Fig. 4. Goat 5. Scoliosis in a goat 7 months of age resulting from unilateral arrestment of growth of second, third, and fourth lumbar vertebræ. Growth was arrested by excising a portion of the right half of both proximal and distal epiphyseal cartilages from these vertebræ at 1 month of age. Note presence of rotation as well as lateral bending, also the wedge-shaped second, third, and fourth lumbar vertebræ and evidence in both photograph and roentgenogram of destruction of the epiphyseal cartilages of these bodies for a depth of approximately one-fourth of their breadths on the side operated upon. An onlay graft consisting of a segment of a rib was placed in contact with exposed cancellous bone of the bodies of the fifth and sixth lumbar vertebræ. Note fixation of these vertebral bodies by a bridge of bone and that this fusion has not disturbed the growth of these bodies.

vertebræ were fused (Fig. 5) and in 1 only 2 vertebræ (Fig. 4).

In addition to these 3 animals in which both growth arrest and fusion operations were carried out, 1 goat was subjected to fusion operations only. These were carried out in 2 stages by fusing the tenth and eleventh thoracic vertebræ at the first operation, and the fourth and fifth lumbar vertebræ at the second operation (Fig. 6). To fuse the thoracic vertebræ a rib graft was used, and to bridge the lumbar segments chip grafts were obtained from the vertebral bodies and from their transverse processes.

In every instance fusion by a firm, bony bridge resulted. Injury to the growth cartilages was carefully avoided. Consequently, growth progressed normally despite the development of a large, solid segment of bone extending between the vertebral bodies and across the growth cartilages (Figs. 4, 5, and 6). Thus fusion by a bony bridge did not interfere with growth. Furthermore, this bony bridge became elongated to accommodate itself to the longitudinal growth of the vertebræ. It is apparent, therefore, that under certain circumstances bone, that is, transplanted bone, is capable of intrinsic growth in length.

Observation showed that these fusions directly between vertebral bodies were very firm and rigid, and the operations were accomplished with comparative ease and without appreciable shock to the animals.

### ANALYSIS OF STUDY

The first step in this investigation was the establishment of the fact that vertebræ grow in length solely from their epiphyseal growth cartilages. With this established it was reasoned that removal or destruction of these growth cartilages would prevent further growth in length of vertebræ so treated; and that if the cartilages were destroyed on one side only, unilateral growth arrest, wedge-shaped vertebral bodies, and lateral deviation of the spine would result. This is precisely what happened; a structural, rotary-lateral curvature was obtained.

It seems logical to assume that the vertebræ of man likewise grow in length solely from the epiphyseal growth cartilages and that unilateral retardation of growth would bend and twist the spine in similar fashion. However, before progressing further with this discussion it is important to recognize the fact that in all comparative investigation of scoliosis in experimental animals one is confronted with the all important influence of posture and the inability in animals to simulate and, therefore, evaluate the influence of the erect posture assumed by man. We see no reason why this fact should in any way detract from the direct application of these experimental observations to comparable findings in man. Structural changes from arrested growth should take place irrespective of the position of the spine; the spine which balances superincumbent weight in a vertical position should develop a curvature with less provocation, and it should bend more extensively and the curvature be more progressive under the same influence than the horizontal spine.

Fig. 5. Spine of a goat 10 months after operative fusion and growth arrest performed before the animal was 1 month of age. Growth was arrested on the right side of first and second lumbar vertebræ through a subdiaphragmatic approach and 1 week later the bodies of ninth, tenth, eleventh, and twelfth thoracic vertebræ were exposed extrapleurally and fused by onlaying grafts of segments of 2 ribs. Note wedging of first and second lumbar vertebræ and the resultant scoliosis, also the firm fusion of the lower thoracic vertebræ and the failure of this fusion to disturb growth of these vertebral bodies.

Fig. 6. Fusions 10 months after operation between the fourth and fifth lumbar and tenth and eleventh thoracic vertebral bodies accomplished in 2 stages. In the thoracic region costal grafts were used and in the lumbar region chips which were removed from the vertebral bodies and their transverse processes. Again fusion did not appreciably disturb growth of these bodies.

The curvatures produced in these experimental animals have much in common with idiopathic scoliosis of man. It is our belief, therefore, that inequality of growth on the 2 sides of the vertebral bodies plays a major rôle in the production and progression of idiopathic scoliosis. If not the primary etiological factor, as it may well be, it is an important contributing factor. This contention is supported by the fact that these curvatures develop only in children and pre-adults, that is, during the period of active growth, and they cease to progress as soon as growth is terminated.

How otherwise can one explain the development of wedge-shaped vertebræ? The only other possible explanation is absorption of bone and compression of the vertebræ on one side. As the spine bends laterally, pressure exerted by the superincumbent weight is shifted and applied principally to the sides of the vertebræ on the side of concavity. Therefore, it may be reasoned that this pressure causes compression and narrowing of the vertebræ on that side. This type of compression is observed in conditions associated with extreme skeletal demineralization or with destruction of the vertebræ. But in the presence of normal mineral metabolism the response of bone to increased stress or pressure is quite the opposite. It responds by reinforcement in accordance with Wolff's law. If wedging does result from pressure absorption and compression, these structural changes should continue to increase after growth ceases and they should develop with curvature arising during adult life. In the scolioses which do arise during adult life, such as those resulting from thoracic disease and operations upon the thorax, the vertebræ develop little or no structural change.

It is more probable that abnormal pressure causes wedging by retarding growth rather than by compression. For example, it may be

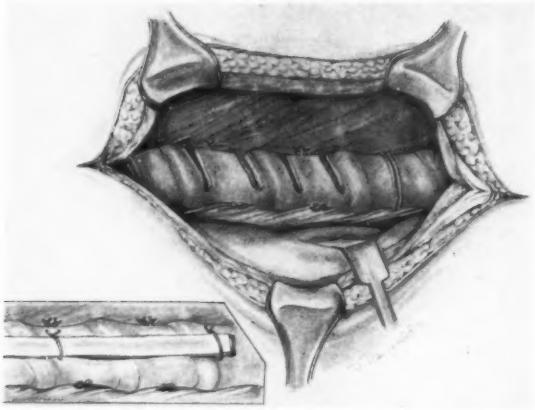

Fig. 7. Retroperitoneal operative approach for exposure of the lumbar vertebral bodies through an incision along the lateral margin of the erector spinæ muscles. The perirenal fat, kidney, peritoneum, and fibers of the psoas muscle are retracted mesially and anteriorly. To avoid troublesome bleeding, the lumbar vessels are divided between ligatures. By incising longitudinally and elevating the common ligaments and periosteum, the bone or growth cartilages can be exposed readily. The method of arresting growth by excising a portion of the epiphyseal cartilages is illustrated. The insert depicts the method of applying a partially inlaid graft to accomplish direct fusion between vertebral bodies.

assumed that the curvature of idiopathic scoliosis is initiated by some factor, such as muscle imbalance, and that as the spine deviates laterally the abnormally increased pressure exerted on the sides of the vertebræ on the concave side of the curvature causes retardation of growth on that side. The consequent wedging of the vertebral bodies contributes to the progression of the curvature. Strong contradictory evidence to this hypothesis is presented by the findings in empyema or pleurogenic scoliosis in children. As pointed out in a previous publication (1), the vertebræ in this type of scoliosis develop little or no structural change despite lateral bending and the vigorous compressing force of the contracting pleural scar. Not infrequently a curvature of this type is corrected completely following a Schede thoracoplasty which, in addition to removing a portion of the thoracic wall, releases the pull of the pleural scar. Such realinement of the vertebræ would be impossible in the presence of significant structural change in the vertebral bodies.

It is equally probable that unilateral retardation of growth is the initiating, as well as the contributing, factor. This is supported by the fact that the fixed structural type of curvature usually does not develop in children whose spines deviate laterally to accommodate for an inequality in the length of the lower extremities. As a rule, curvatures of this type increase only as the inequality in the length of the legs increases and the spine immediately straightens when this inequality is corrected and the pelvis made horizontal by raising the short leg.

In paralytic scoliosis of anterior poliomyelitis in children the vertebræ frequently become wedge-shaped. Unquestionably these structural changes result from unilateral retardation of growth and for the same reason that growth is retarded in paralytic extremities. Shortening in paralyzed extremities is attributed to disuse and to trophic influences. Both of these factors, we believe, exert their influence through the vasomotor mechanism, so that the fundamental cause of the growth retardation is the diminution in the blood supply of the growth cartilage. Each lateral half of the vertebral body has an independent blood supply received from nutrient vessels which enter the body to the left and right of the midline. These nutrient vessels are branches of their respective left and right intercostals in the thoracic region and of the right and left lumbar vessels below the diaphragm. Thus, from the standpoint of circulatory influence, the vertebral bodies may be bisected into right and left halves and upon this basis unilateral growth retardation in these paralytic cases may be explained.

The curvatures of paralytic scoliosis are inconstant in respect to the direction in which they deviate, that is, the convexity may be directed to the side with either the weaker or the stronger muscles. However, when structural changes are present in the vertebræ, the

Fig. 8. Extrapleural approach to the thoracic vertebral bodies Short segments of 2 ribs are resected from the costotransverse articulations laterally. Through the rib beds the endothoracic space is carefully entered and the parietal pleura dissected from the thoracic wall and retracted mesially and anteriorly, thus exposing the vertebral bodies. The intercostal vessels are divided between ligatures and the common ligaments and periosteum incised longitudinally, elevated, and retracted. Illustrated is the method of arresting growth.

convexity will be found on the stronger side and the changes from retarded growth on the weaker or more completely paralyzed side.

If unilateral growth retardation is the sole factor responsible for idiopathic scoliosis, what causes this unilateral retardation of growth? Among the theoretically possible causes are epiphysitis or epiphyseodystrophy and congenital abnormality of the cartilage. The latter possibility is suggested by an observation made by Chandler, who has noted that children with idiopathic scoliosis frequently present maldevelopment of the mandible.

### GROWTH CORRECTION OF SCOLIOSIS

From the above experimental evidence that growth on one side of vertebræ can be arrested by removal of portions of the epiphyseal growth cartilages on that side, the possibility of accomplishing correction of curvatures of idiopathic scoliosis in suitable cases by this means suggests itself. The type of case which would seem suitable for this proposed form of treatment would be a child who has a moderate curvature and several years in which to grow. With growth arrested on the side of

Fig. 9. Diagrammatic illustration of a scoliotic spine in which segments of both distal and proximal growth cartilages have been excised on the side of convexity of 5 vertebræ at the apex of the curvature. The resultant growth arrest on the side of convexity should retard progression of the curvature; and if length is gained from growth on the opposite side of these vertebræ, some correction of the curvature should take place.

convexity in several vertebræ at or near the apex of the curvature, any increase in length on the side of concavity should bring about some correction of the curvature.

As to the accessibility of the vertebral bodies in man, I may state that in performing the operations of Peet and of Craig for essential hypertension we have always exposed several vertebral bodies both above and below the diaphragm; and this has been accomplished without technical difficulty or appreciable shock to the patients.

In patients with scoliosis, exposure of vertebral bodies should be accomplished more easily, because on the side of the convexity the ribs are abnormally widely separated and the vertebral bodies are near the surface. With the resection of segments of 2 ribs it should be possible to expose 6 or more of the vertebral bodies.

In goats the centers of ossification for the epiphyses appear early; there were well formed epiphyses at the time of operation, which was as early as 2 weeks after birth. In man these centers appear at about the seventeenth year and fuse with the diaphysis during the twentieth year of life. Thus to accomplish growth arrest in performing the proposed operation for growth correction of scoliosis in children it would be necessary to excise the full thickness of the cartilage from the diaphysis to the intervertebral disc on one side.

### FUSION OF VERTEBRAL BODIES

Under certain limited circumstances it would seem feasible to apply the method of direct fusion of vertebral bodies clinically by means of onlay grafts as demonstrated in the experimental studies here discussed. It would be applicable only in those cases in which there was no vertebral infection and in which it was necessary to fuse not more than 4 vertebræ. Among such possible indications are certain old compression fractures and high spondylolithesis—above the fifth lumbar vertebra.

### CONCLUSIONS

1. In goats and presumably in man, all growth in the length of vertebræ is derived from the proximal and distal epiphyseal growth cartilages. An equal increment is received from each cartilage.

2. Excision of the epiphyseal growth cartilages results in arrestment of growth in length. Unilateral excision causes unilateral growth arrest.

3. The production of rotary lateral curvatures of the spine in goats by unilateral growth arrest of 2 or 3 vertebræ is reported.

4. Both experimental and clinical observations are presented as evidence that unilateral retardation of growth of vertebræ is either totally, or at least partially, responsible for idiopathic scoliosis of man.

5. Fusion of vertebral bodies *per se* with no damage to the epiphyseal cartilages does not arrest growth.

6. Under the influence of a distracting force, bone, that is, grafted bone, is capable of intrinsic growth in length.

7. Methods for growth correction of scoliosis and for direct fusion of vertebral bodies are proposed.

Since this paper was received for publication there has appeared a report of similar experimental studies by S. L. Haas, J. Bone & Joint Surg., 1939, 21: 963. In general our results agree with those of Haas.

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# CANCER OF THE THYROID

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CANCER of the thyroid is an exceptional disease in that it fails to follow the general tumor behavior laws, and its reaction to surgical and radiation therapy is quite unique. Even though a wealth of operative material has been studied histologically, there is no tumor in the head and neck group which seems to present more diagnostic problems for the tumor pathologist. All tumor gradations from benignity to malignancy are noted in addition to the six histologically definite cancer groups used in this report.

In order that the resulting statistics and conclusions may have some factual value, we have excluded from consideration all records in which microscopic evidence of true thyroid cancer is lacking. In most of the early cases biopsies were not done, as it was considered a dangerous procedure. Not until 1928 was any very consistent effort made in each case to confirm the clinical diagnosis by histological study, so that although 973 patients with tumors of thyroid origin have been admitted to Memorial Hospital, and at least 248 of these were clinically cancerous, in only 167 instances do we have histological evidence as to the cellular type of the cancer and its histological grade. This series of thyroid cancers comprises 0.43 per cent of the general admissions to our institution.

## MATERIAL

Fifty per cent of our patients had received pre-admission surgical treatment (83 of 167—Table I). An additional 5 per cent had received medical treatment, and only 25 per cent (42 of 167) received their primary therapy at Memorial Hospital. Many cases hopelessly advanced were sent to us for any possible palliative radiation therapy (Fig. 1). All patients hopeless or otherwise were accepted for treatment if they were ambulatory, and if bedridden they were accepted up to the bed capacity of the hospital. Obviously, it will be more difficult to demonstrate satisfactory end-results with this material than with the straight surgical series in which 60 per cent of the thyroid cancers are so small and well encapsulated as not to be suspected before thyroidectomy (Pemberton). In other words, the easily curable cases are unsuspectingly cured by routine surgical procedures in the average surgical clinic. To summarize the material admitted to Memorial Hospital, we find that 50 per cent of the patients had received previous surgical attention, 70 per cent were considered as inoperable, 37 per cent presented evidence of metastatic thyroid cancer, and 44 per cent showed evidence of obstruction to the upper food or air passageways (Table II).

Cancer of the thyroid occurs more frequently in females, the proportion in this series being 117 females to 50 males, roughly 2 to 1 (Fig. 2). The majority of cases occur in the age groups of 40 to 60. The youngest patient was a boy of 9 years of age and the oldest a female of 86 who had a bulky cancer of lingual thyroid origin. She is now alive and well at the age of 91 (Fig. 3).

Regardless of our large metropolitan negro and oriental population, only 4 patients in this series were negroes and only 1 came from the Orient. As to foreign birthplace, Russians, Germans, and Italians predominated in that order (Table III).

The primary tumor was confined to one lobe of thyroid gland in 87 cases (48 right lobe and 39 left lobe). The isthmus alone was involved 8 times and the growth involved both lobes in 50 cases, with substernal extension of disease being noted 18 times (Table IV). In several cases presenting extensive unilateral or bilateral cervical chains of thyroid cancer, we suspected the process of having developed from multiple sites in aberrant thyroid rests, but as small, unsuspected, pri-

From the Head and Neck Department, Memorial Hospital, service of Dr. Hayes E. Martin.

Presented at the Third International Cancer Congress, Atlantic City, New Jersey, September 11-16, 1939.

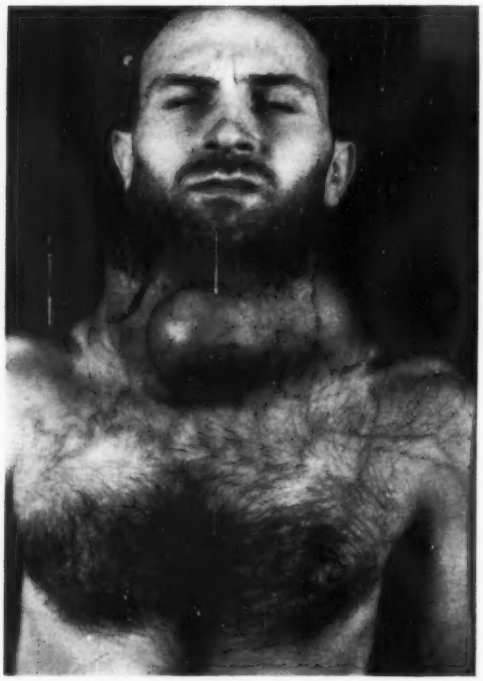


Fig. 1. Advanced cancer of thyroid (small alveolar adenocarcinoma). Infrared photograph to show dilated venous plexus resulting from tumor obstruction of the internal jugular veins. An inoperable case accepted for palliative radium pack therapy.

mary foci of cancer were found in the thyroid gland itself at operation, our original contention had to be withdrawn and in only one questionable case is an aberrant nature of the primary disease suspected. In 3 instances primary cancer developed in lingual thyroid tissue.

TABLE I.—PREVIOUS TREATMENT

| | No. cases |
|---|---|
| Surgical | 53 |
| X-ray therapy | 12 |
| Surgery and x-ray therapy | 9 |
| Surgery and radium | 5 |
| Biopsy | 13 |
| Tracheotomy | 1 |
| Enucleation | 2 |
| Medical (iodine, thyroid extract, ice packs, etc.) | 8 |
| No treatment | 42 |
| Not stated | 22 |
| | 167 |

Nearly 75 per cent of the cases of thyroid cancer admitted to Memorial Hospital have had previous treatment. Fifty per cent had inadequate surgical treatment elsewhere.

### ETIOLOGY

As to the etiology of cancer of the thyroid, we find in our study nothing which definitely points to a specific cancerogenic agent.

### HISTOLOGY

Recognizing the many histological variations of thyroid cancer, it has been our aim to classify these growths into as small a number of groups as possible, and, with this in mind, Dr. F. W. Stewart has reviewed the pathological material used in this report and again points out the difficulty in differentiating between benign and malignant thyroid growths. For this reason, all questionable cases were classed as benign. Somewhat arbitrarily we selected the following 6 major types of thyroid cancer, each of which presents its own more or less typical histological and clinical characteristics. This grouping is practically the same as that suggested by Haagensen.

First, and occurring most frequently—34 per cent of the cases—is the papillary adenocarcinoma (Fig. 4). This tumor is moderately radiosensitive, invades neighboring structures, and metastasizes frequently to the regional lymph nodes, but practically never to distant structures by way of the blood stream. Histologically, the tumor presents a network of branching papillæ projecting into cystic cavities which may contain a gelatinous substance. The papillæ are lined with a single or multiple layer of cuboidal or cylindrical epithelial cells.

In the second group are the small alveolar, large cell adenocarcinomas which make up 27 per cent of the series (Fig. 5). The structural feature common to this group is the alveolar arrangement of compact masses or cords of

TABLE II.—FIRST SYMPTOM—167 CASES

| | No. cases |
|---|---|
| Lump in thyroid (goiter) | 100 |
| Lump in neck (cervical metastasis) | 38 |
| Bone pain, dysphagia, dyspnea, etc. (distant metastasis) | 25 |
| Not stated | 4 |

First symptom was due to metastases in 63 cases (37%) of this series

Primary cancer of the thyroid gland may be quiescent for years and in one-third of our cases the patient's first symptom was produced by metastatic deposits of the disease.

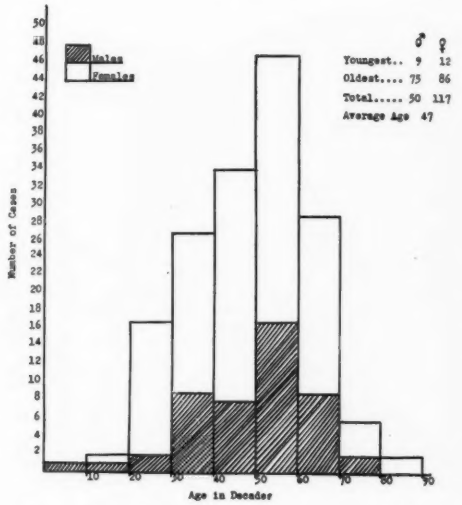



Fig. 2. Thyroid cancer occurs in females twice as frequently as in males. The largest group of patients were between 50 and 60 years of age.

Fig. 3. M. Y. Showing a large bulky thyroid cancer having its origin from embryonic thyroid tissue at the base of the tongue. Patient 86 years of age, now alive and well at age of 91.

cells. Adult alveoli containing colloid are seen and the cell cytoplasm is slight in amount, opaque, and granular, and stains heavily with eosin. These growths are only slightly radiosensitive; they grow rather rapidly, reaching a huge size and soon cause dysphagia and dyspnea. They metastasize regularly through blood and lymph channels.

Spindle and giant cell adenocarcinomas have been placed in the third group. They comprise 13 per cent of the series (Fig. 6). These neoplasms are extremely malignant, quite radioresistant, metastasize widely to cervical nodes and distant areas, and are rapidly fatal. The histological picture is that of irregularly growing sheets or strands of very anaplastic, hyper-

TABLE III.—RACE AND BIRTHPLACE IN A SERIES OF 167 CASES

| | |
|---|---|
| Race | |
| Caucasian | 161 |
| Negro | 4 |
| Oriental | 1 |
| Not stated | 1 |
| | 167 |
| Birthplace | |
| United States | 67 |
| Russia | 38 |
| Italy | 14 |
| Germany | 8 |
| Austria | 8 |
| Ireland | 7 |
| Poland | 4 |
| Roumania | 3 |
| Hungary | 3 |
| France | 2 |
| British West Indies | 1 |
| Honolulu | 1 |
| Turkey | 1 |
| Canada | 1 |
| Spain | 1 |
| Czechoslovakia | 1 |
| Not stated | 7 |
| | 167 |

Our patients were largely of the white race. Only 4 negroes and 1 oriental have received treatment for thyroid cancer at Memorial Hospital.

TABLE IV.—LOCATION OF PRIMARY TUMOR—167 CASES

| | No. cases |
|---|---|
| Right lobe | 48 |
| Left lobe | 39 |
| Bilateral | 50 |
| Isthmus | 8 |
| Lingual | 3 |
| Aberrant (?) | 1 |
| Pyramidal lobe | 1 |
| Not stated | 17 |

Substernal extension of disease was noted in 18 cases.

Thyroid cancer shows a definite tendency to involve both lobes of the gland. Adenocarcinoma having its origin in aberrant thyroid tissue occurred only once.

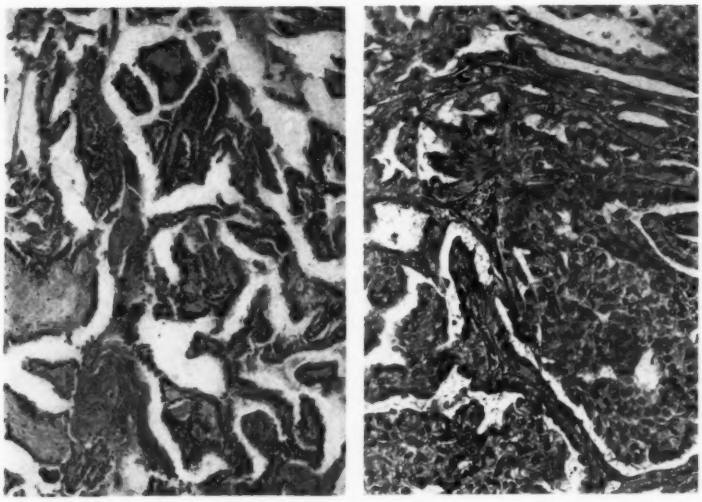


Fig. 4. Papillary adenocarcinoma, grade 1. This type of cancer occurred in 34 per cent of our cases.

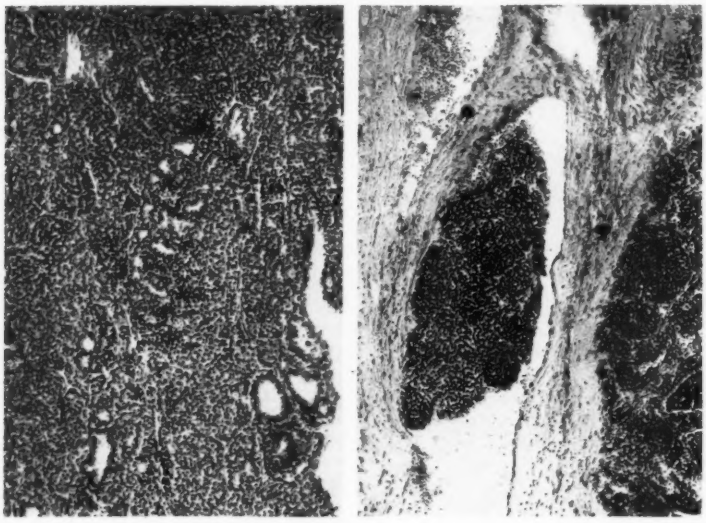


Fig. 5. Small alveolar and solid adenocarcinoma, grade 3, with vein invasion. This type of cancer occurred in 27 per cent of our cases.

chromatic cells varying greatly in size and shape. The largest cells are somewhat fusiform in shape and these form the so called giant cells.

The fourth group comprises those cases designated as small round cell carcinomas (Fig. 7). Five per cent of the series was so classified. These tumors are most malignant. Death

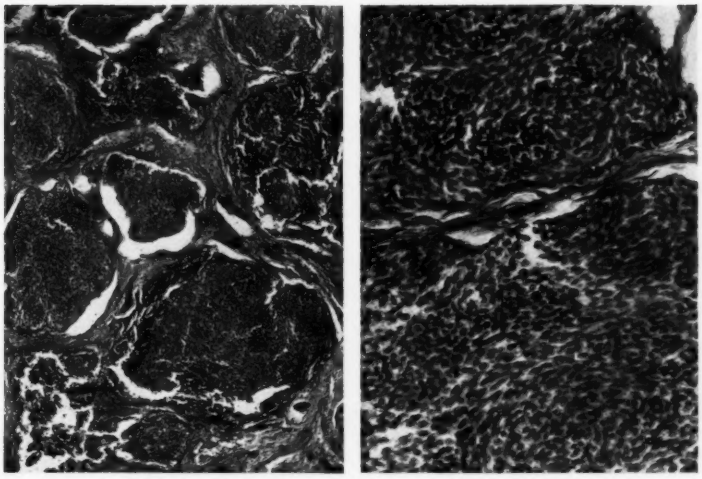


Fig. 6. Spindle cell and giant cell adenocarcinomas made up 13 per cent of the series.

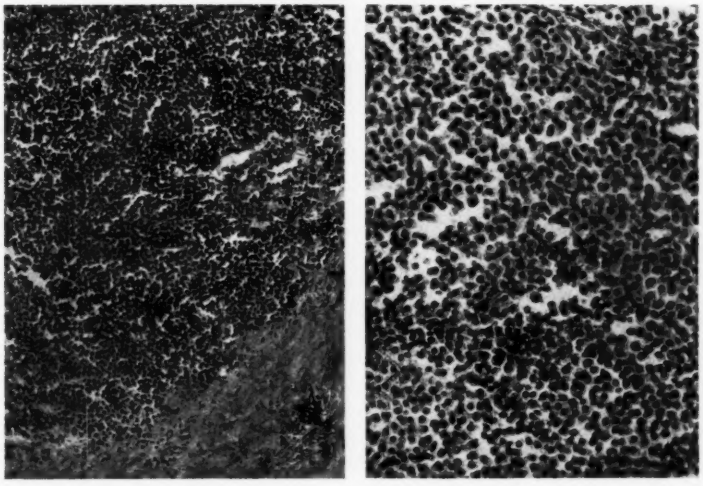
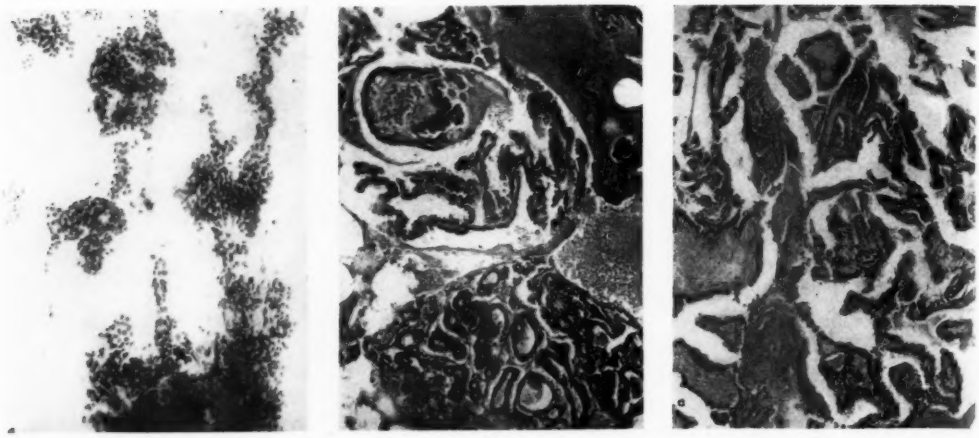


Fig. 7. Small round cell carcinoma, grade 4. This histological group made up 5 per cent of our series.

occurs rapidly as a result of widespread visceral metastases. The tumors are not radiosensitive, they are composed of rather loosely arranged small round cells growing diffusely and infiltrating capsule and surrounding tissues.

Lymphosarcoma primary in the thyroid gland was noted in 5 of our cases, and they make up our fifth group and 3 per cent of the series. These lesions are very radiosensitive.

The sixth group contains 5 cases which Dr. Stewart has classified as metastasizing struma. These tumors make up 3 per cent of our series and represent those cases in which thyroid metastases were histologically proved but the sections of thyroid gland tissue submitted



a b c

Fig. 8. Photomicrographs of an aspiration biopsy. a, The smeared material. b, The section of the aspirated clot. c, Formal histological section of the tumor removed at operation.

showed merely benign goiter or adenoma, and no definite cancer. Serial sections might have located a primary cancer. The histological groups and grades of thyroid cancer are summarized in Table V.

TABLE V.—PATHOLOGY—167 CASES

| | | No. cases | Per cent |
|---|---|---|---|
| Papillary adenocarcinoma | | | |
| Grade 1 | 47 | | |
| Grade 2 | 8 | | |
| Grade 3 | 2 | | |
| Total | | 57 | 34 |
| Small alveolar and solid, large cell adenocarcinoma | | | |
| Grade 2 | 28 | | |
| Grade 3 | 12 | | |
| Huerthle-cell type | 5 | | |
| Total | | 45 | 27 |
| Adenocarcinoma, ungraded | | 24 | 15 |
| Spindle and giant cell carcinoma | | | |
| Grade 3 | 20 | | |
| Grade 4 | 3 | | |
| Total | | 23 | 13 |
| Small round cell carcinoma | | | |
| Grade 2 | 2 | | |
| Grade 3 | 1 | | |
| Grade 4 | 5 | | |
| Total | | 8 | 5 |
| Metastasizing struma | | 5 | 3 |
| Lymphosarcoma | | 5 | 3 |
| | | 167 | |

This table shows the histological grouping and tumor grades used in this series of 167 cases of thyroid cancer.

DIAGNOSIS

Making an accurate pre-operative diagnosis in the early case of thyroid cancer is always difficult and in a certain group it is often quite impossible, but in the later and advanced stages of the disease the diagnosis is as obvious as the prognosis is poor (Table VI).

Clinically it is often quite difficult to differentiate between a benign adenoma and cancer. In our series of 62 primary operable cases of thyroid cancer, there were 11 instances, 18 per cent, in which the surgeon had made an inaccurate pre-operative diagnosis of thyroid adenoma. Aspiration biopsies have been a considerable aid to us in establishing an accurate pre-operative diagnosis (Fig. 8). During the first years of this procedure's popularity at Memorial Hospital, it was considered quite difficult to interpret thyroid aspirations (Martin). This is still true, but by comparing smears of aspirated material with the sections of the excised thyroid mass, Dr. Stewart has considerably increased the accuracy of his reports on thyroid aspirations (Fig. 9). Negative reports mean, of course, absolutely nothing. In the series we examined, 74 aspiration biopsies were attempted and the report was positive for cancer in 62 cases and negative in 12. A pre-operative test for cancer which is positive in 83 per cent of the cases seems definitely of value. In the present group of

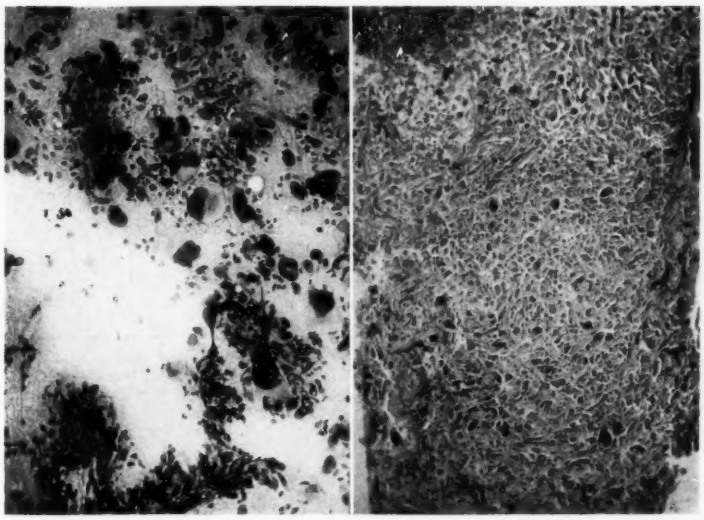


Fig. 9. Smear and sectioned clot of aspiration biopsy. Spindle and giant cell carcinoma, grade 3. In the pre-operative differential diagnosis of thyroid cancer, aspiration biopsies such as this established a definite diagnosis of cancer in 83 per cent of the cases in which it was attempted.

patients, there were 2 instances in which formal surgical biopsy had been carried out before admission and indefinite material obtained. Aspiration biopsy established the diagnosis of thyroid cancer in each of these cases. If one has a positive pre-operative diagnosis, it is much easier to plan the proper treatment and carry out, with a clear conscience, a long, difficult, and cosmetically unpleasant operation which will change the contour of the patient's neck, paralyze the trapezius muscle and considerably alter the speaking voice.

Frozen section at operation is mentioned here only to state that in our hands it has been unreliable. We have had several reports of "no cancer" when later sections demonstrated the presence of definite neoplastic tissue. We believe the experienced cancer surgeon, when impressed at operation with the possibility that he is dealing with cancer, is justified in proceeding with a suitable type of operation regardless of the frozen section and aspiration biopsy reports.

## TREATMENT

In discussing therapeutic measures for the management of the patient with cancer of the thyroid, a number of individual circumstances and conditions must be considered and treatment altered accordingly. But, examining the problem from a broad viewpoint, it seems well established that surgery and radiation will play complementary rôles in the proper care of patients with this disease. This attitude is shared by the larger American clinics doing this work (Pemberton, Lahey, Crile). Several years ago, while operating for cancer of the thyroid and applying to the problem principles which have been found acceptable for radical neck dissection in general, it became necessary to carry out the following operative procedure which we feel is worthy of reporting. As to anesthesia (Table VII) our opinions are definite. We have tried rectal, intravenous, and inhalation anesthesias for neck dissection

TABLE VI.—SIXTY-TWO PRIMARY OPERABLE CASES

| Pre-operative diagnosis.— | Cases | Per cent |
|---|---|---|
| 1. Adenoma | 11 | 18 |
| 2. Carcinoma | 51 | 82 |

In a series of 62 primary operable cases of thyroid cancer, the operating surgeon made an inaccurate pre-operative diagnosis of benign adenoma in 11 cases.

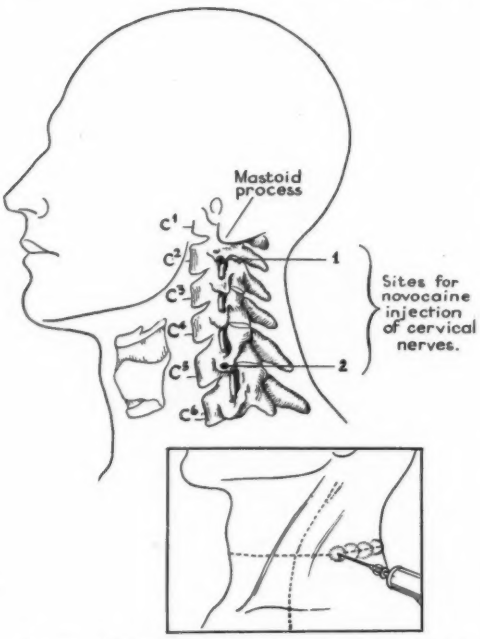



Fig. 10. Novocain anesthesia is used exclusively. Cervical nerve block with 1 per cent novocain is carried out by the Labat technique and the line of incision is infiltrated with 1 per cent novocain containing 10 drops of adrenalin in the first ounce. (After Labat.)

and discarded each in favor of novocain local infiltration and cervical nerve block anesthesia (Fig. 10), and to this we attribute the fact that in a series of 12 radical thyroidectomies combined with neck dissection, no postoperative death has occurred.

As the operation is to be carried out under local anesthesia (Labat) the patient must be draped in such a fashion as to permit free breathing (Fig. 11). In a protracted operation such as this one, a sense of suffocation produced by heavy sheets too close to the mouth and nose makes the patient apprehensive and uncomfortable, and, when the surgeon has cut

TABLE VII.—ANESTHESIA

| | No. cases | Per cent |
|---|---|---|
| Operations under local anesthesia | 73 | 84 |
| Operations under general anesthesia | 14 | 16 |
| Total | 87 | |

Local anesthesia is preferred for both minor and major thyroid surgery in 84 per cent of the cases.

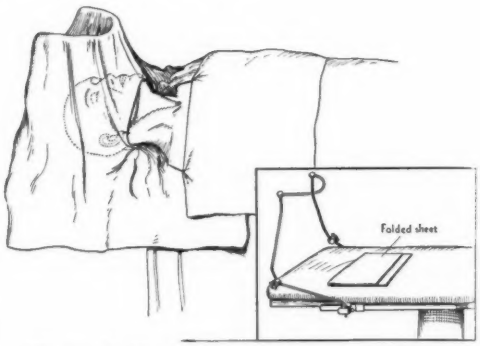



Fig. 11. Position of patient with drapes. As the operation is performed under novocain anesthesia, a method of draping is necessary which fulfills sterile precautions and yet permits the patient to breathe normally and allows the surgeon and his assistants adequate elbow room.

the recurrent laryngeal nerve and is dissecting the tumor from the trachea, there will be less technical difficulty if the patient is not struggling for air. A satisfactory drape must also permit the surgeon and his assistants adequate elbow room.

An incision is selected which will provide the widest exposure for the individual case (Fig. 12). A generous expo ure is necessary for safety and for complete removal of the disease and the potentially involved veins and lymph nodes.

The operative procedure which we favor consists of three major steps. First (Fig. 13), the sternomastoid muscle is cut across at its upper third and the internal jugular vein above the superior thyroid vein is doubly ligated and sectioned. This considerably decreases subsequent bleeding. The sternomastoid muscle is then severed close to its bony origins and the internal jugular vein clamped and doubly ligated and severed just above the angulus venosus. The lowest thyroid veins are also ligated and severed.

The second step (Fig. 14) consists mainly in sectioning the sternohyoid and sternothyroid muscles at their origins and insertions. At this point the posterior cervical triangle and the retrosternal spaces are dissected free of all lymph nodes and surrounding fatty and areolar tissue.

The third step (Fig. 15) consists in dissecting the internal jugular vein and its chain of

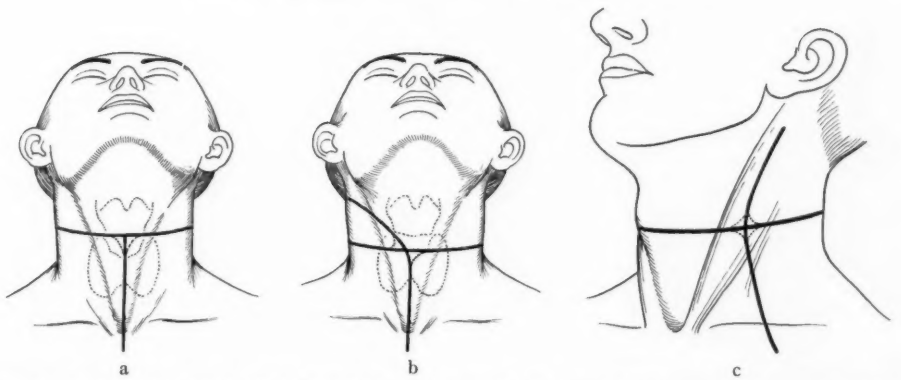


Fig. 12. a, Incision. A high collar incision at the level of the cricoid cartilage extending to the lateral borders of both sternomastoid muscles. A vertical limb bisects this and continues downward to the suprasternal notch. b, A high collar incision bisected by a curved incision from the tip of the mastoid process to the suprasternal notch. c, A high, wide collar incision bisected by a curved incision from the tip of the mastoid process to the midclavicle. This permits ready access to the posterior cervical triangle and subclavian space.

nodes free from the vagus nerve and common carotid artery (Watson)—these structures may be sacrificed if invaded—then cutting across normal thyroid at a safe point and removing the entire mass from the trachea and esophagus by sharp dissection. The recurrent laryngeal nerve is always sacrificed. The wound is drained with three or four large cigarette drains, platysma and skin closed, and a large sea sponge pressure dressing applied.

### OPERATIVE MORTALITY

Eighty-six patients had a total of 104 operations and of this group 51 cases could be classified as primary operable and 1 patient, a total thyroidectomy, died after operation. In the 12 instances in which radical thyroidectomy with neck dissection was carried out, there was not a single operative death (Table VIII).

The palliative operative procedures for temporary relief of dyspnea and dysphagia resulting from advanced thyroid cancer are attended by a high operative mortality. Tracheotomy, for example, was followed by death in 50 per cent of 14 late cases in which it was carried out in attempting to relieve dyspnea.

Before an operation for thyroid cancer is started, we elect to have at hand in the operating room a sufficient quantity of interstitial radon for our needs in case the tumor cannot be removed. For a large growth this means at least 70 millicuries, preferably in seeds of about 2 millicuries each. Large doses of interstitial radon can be used with safety if the seeds are carefully distributed so as not to concentrate the reaction and produce necrosis of vital structures. The larger the excised portion of tumor, the smaller the total amount of radon which will be necessary for control of the irremovable portion. Having large amounts of radon at the surgeon's disposal is one advantage offered to the patient by the well equipped modern cancer institute.

TABLE VIII.—OPERATIVE MORTALITY—86 PATIENTS—104 OPERATIONS

| Operation | No. cases | No. deaths | Per cent |
|---|---|---|---|
| Partial thyroidectomy | 28 | 0 | |
| Partial thyroidectomy and excision of nodes | 7 | 0 | |
| Total thyroidectomy | 3 | 1 | 33 |
| Radical thyroidectomy | 12 | 0 | |
| Radical neck dissection | 1 | 0 | |
| Biopsy and exploration | 4 | 1 | 25 |
| Decompression | 8 | 1 | 13 |
| Excision of recurrences | 10 | 1 | 10 |
| Exposure of node and implantation of radon | 15 | 1 | 7 |
| Tracheotomy | 14 | 7 | 50 |
| Gastrostomy | 1 | 1 | 100 |
| Excision of tumor base of tongue | 1 | 0 | |
| | 104 | 13 | |

In a series of 51 radical procedures for thyroid cancer, 1 patient died—less than 2 per cent operative mortality. The palliative operations resulted in a high mortality.

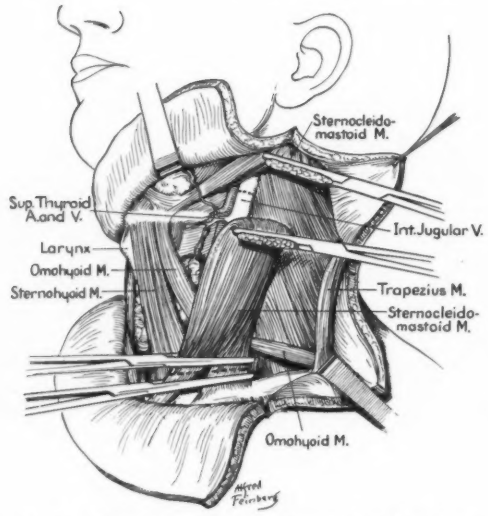



Fig. 13. Step 1. The skin and platysma flaps have been dissected up and the sternomastoid muscle cut across at the hyoid level. The upper site of ligation of the internal jugular vein is indicated. The incision across the clavicular portion of sternomastoid muscle is shown.

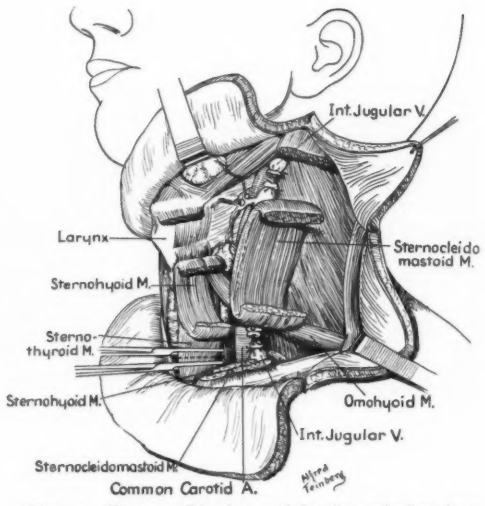



Fig. 14. Step 2. The internal jugular vein has been ligated and cut above and below. The prethyroid muscles are being cut across well above and below the tumor. The substernal and supraclavicular spaces are dissected at this stage.

If postoperative radiation is to be given, we recommend divided doses of x-ray therapy given with a 200 kilovolt machine having a filter of ½ millimeters copper and 1 millimeter aluminum. The treatments are given through a portal about 14 by 7 centimeters placed obliquely along the operative side of the neck from the angle of the mandible to the suprasternal notch. Treatments of 200 roentgens are given every 2 days for a total of about 3,000 roentgens. We believe postoperative irradiation to be effective should be pushed up to a dose sufficient to kill cancer cells if they remain. The mild postoperative "x-ray cycle" has no place in the management of thyroid cancer.

TABLE IX.—PRIMARY REGRESSION AFTER PRIMARY RADIATION—81 CASES

| Pathology | No. cases | Degree of regression | | | | |
|---|---|---|---|---|---|---|
| | | None % | Slight % | Moderate % | Marked % | Complete % |
| Small alveolar and solid adenocarcinoma | 24 | 46 | 13 | 29 | 8 | 4 |
| Papillary adenocarcinoma | 22 | 45 | 18 | 5 | 14 | 18 |
| Spindle and giant cell adenocarcinoma | 17 | 53 | 12 | 23 | 6 | 6 |
| Unclassified adenocarcinoma | 12 | 34 | 16 | 8 | 34 | 8 |
| Lymphosarcoma | 3 | — | — | — | 33 | 67 |
| Metastasizing goiter | 2 | — | 100 | — | — | — |
| Small round cell carcinoma | 1 | 100 | — | — | — | — |
| Total | 81 | 43 | 15 | 17 | 14 | 11 |

Papillary adenocarcinoma of thyroid origin is fairly radiation sensitive. Other types, however, are not sensitive to the usual radiation measures.

### RADIOSENSITIVITY OF THYROID CANCER

In 81 cases in which it was possible to judge the effect of primary radiation on thyroid cancer, it was noted that 32 per cent of the papillary adenocarcinomas responded well to radiation therapy and all the lymphosarcomas showed marked or complete primary regression of disease, but the patients all died of their disease. The other histological types were for the most part quite radioresistant, this quality being most marked in the spindle and giant cell forms of this disease (Table IX).

### METASTASES

When metastases to the lung and skeleton have occurred and pain becomes a serious fac-

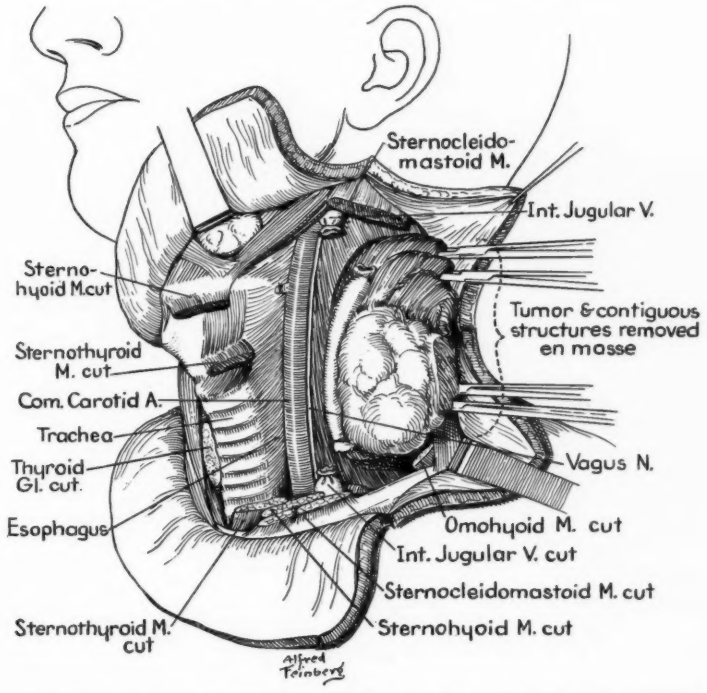



Fig. 15. Step 3. The thyroid tumor with its prethyroid muscles, the internal jugular vein, sternomastoid muscle, and contents of the substernal and supraclavicular spaces are removed *en masse*.

tor, much relief can be obtained by the judicious use of high voltage x-ray therapy. Advanced thyroid cancer gives rise to widespread metastases (Fig. 16) in a considerable percentage of the cases. Seventy-eight per cent of the series presented developed metastases at some time during the course of their disease. Bony metastases occurred in 42 cases (Table X) and lymph node and visceral metastases were noted in 130 instances (Table XI).

A series of 13 cases of thyroid cancer have come to autopsy and the cause of death in 11 was asphyxia resulting from tumor invasion or compression of the trachea. Widespread visceral and bony metastases caused 1 death, and the thirteenth patient with generalized metastases died as a result of hemorrhage from an ulcer of the nasopharynx resulting from advanced cachexia.

A peculiar, low grade, persistent, spiking fever is often noted in the advanced stages of

TABLE X.—PATHOLOGY OF PRIMARY LESION IN 42 CASES WITH BONE METASTASES

| Pathological type | Total cases | Vertebræ | Pelvis | Skull | Ribs | Sternum | Femur | Scapula | Clavicle |
|---|---|---|---|---|---|---|---|---|---|
| Papillary | 12 | 3 | 6 | 1 | 4 | 0 | 2 | 0 | 0 |
| Small alveolar type | 15 | 10 | 2 | 5 | 2 | 4 | 1 | 1 | 2 |
| Adenocarcinoma, unclassified | 7 | 3 | 2 | 1 | 1 | 3 | 2 | 1 | 0 |
| Spindle and giant cell | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Small round cell | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| Metastasizing struma | 3 | 3 | 0 | 1 | 0 | 0 | 1 | 0 | 0 |
| Lymphosarcoma | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 42 | 21 | 10 | 9 | 8 | 7 | 6 | 3 | 2 |

All types of thyroid cancer may metastasize to bone but the small alveolar adenocarcinoma is most prone to do so.

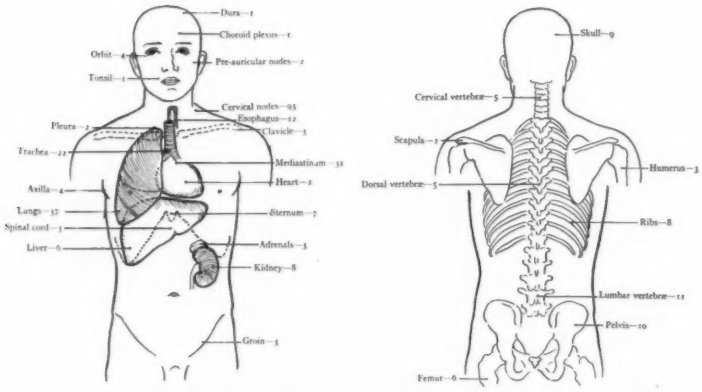



Fig. 16. Showing the site of metastasis from thyroid cancer. One hundred and thirty of the entire series of 167 cases developed metastases at some time during the course of the disease.

thyroid cancer. Especially is this true when widespread metastases are known to exist. Basal metabolism rates taken on our patients with widespread visceral and bony metastases from thyroid cancer failed to show any consistent trend; some were normal, while others showed moderate plus or minus readings.

### CASE REPORT

Mrs. R.B., age 29, white, born in the United States was admitted to Memorial Hospital Clinic July 21, 1938, for diagnosis and treatment. Her chief complaints at that time were "lumps" in the neck and fatigue of 18 months' duration.

Eighteen months before admission to the hospital patient developed a small lump in the right side of her neck. This increased slowly in size and others appeared in both the right and left sides of her neck. Some time later she developed a sense of pressure in the neck and on several occasions noted pain in the right side. She gained about 13 pounds in weight in 8 months. The patient had always been in good health, but she had had a laparotomy for ovarian cyst in 1932. Twenty-one months before admission to the hospital she gave birth to a baby after a normal pregnancy.

On examination the right side of the neck was found to be diffusely enlarged, especially the lower third. This was brought about by a mass of discrete nodes lying for the most part underneath the sternomastoid muscle. The nodes were firm, discrete, and varied in size. The largest one was about 3 centimeters in diameter and the smallest one was about 1 centimeter in diameter. One node was fairly firmly attached to the right side of the trachea. The thyroid was diffusely enlarged but soft.

*Laboratory data.* One of the right neck nodes was removed October 10, 1938 and microscopic examination of the tissue revealed "papillary adenocarcinoma of unusual structure, suggesting branchiogenic rather than thyroid origin." Her blood Wassermann was negative. X-ray films of the chest were negative for metastases.

*Treatment.* The patient was admitted to Memorial Hospital November 15, 1938 for a radical right neck dissection. This was performed under local infiltration and cervical nerve block anesthesia with 1 per cent novocain. A slightly curved incision was made extending from the mastoid region down to the midportion of the clavicle, the convexity of the curve

TABLE XI.—PATHOLOGY OF PRIMARY LESION IN 130 CASES WITH LYMPH NODE AND VISCERAL METASTASES

| Pathological type | Total cases | Cervical nodes unilateral | Cervical nodes bilateral | Other lymph nodes | Mediastinum | Lungs | Trachea and larynx | Esophagus | Liver | Other viscera |
|---|---|---|---|---|---|---|---|---|---|---|
| Papillary | 41 | 18 | 12 | 6 | 7 | 8 | 1 | 2 | 0 | 0 |
| Small alveolar type | 35 | 16 | 7 | 0 | 1 | 14 | 4 | 3 | 4 | 8 |
| Adenocarcinoma, unclassified | 20 | 7 | 7 | 0 | 11 | 3 | 2 | 2 | 1 | 2 |
| Spindle and giant cell | 19 | 10 | 1 | 1 | 6 | 7 | 5 | 3 | 2 | 3 |
| Small round cell | 8 | 3 | 3 | 0 | 2 | 1 | 0 | 0 | 1 | 1 |
| Metastasizing struma | 3 | 2 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 |
| Lymphosarcoma | 4 | 1 | 3 | 1 | 1 | 0 | 1 | 1 | 0 | 1 |
| Total | 130 | 57 | 34 | 8 | 36 | 35 | 13 | 11 | 8 | 15 |

All types of thyroid cancer may metastasize to regional lymph nodes but papillary adenocarcinoma is the most frequent offender.

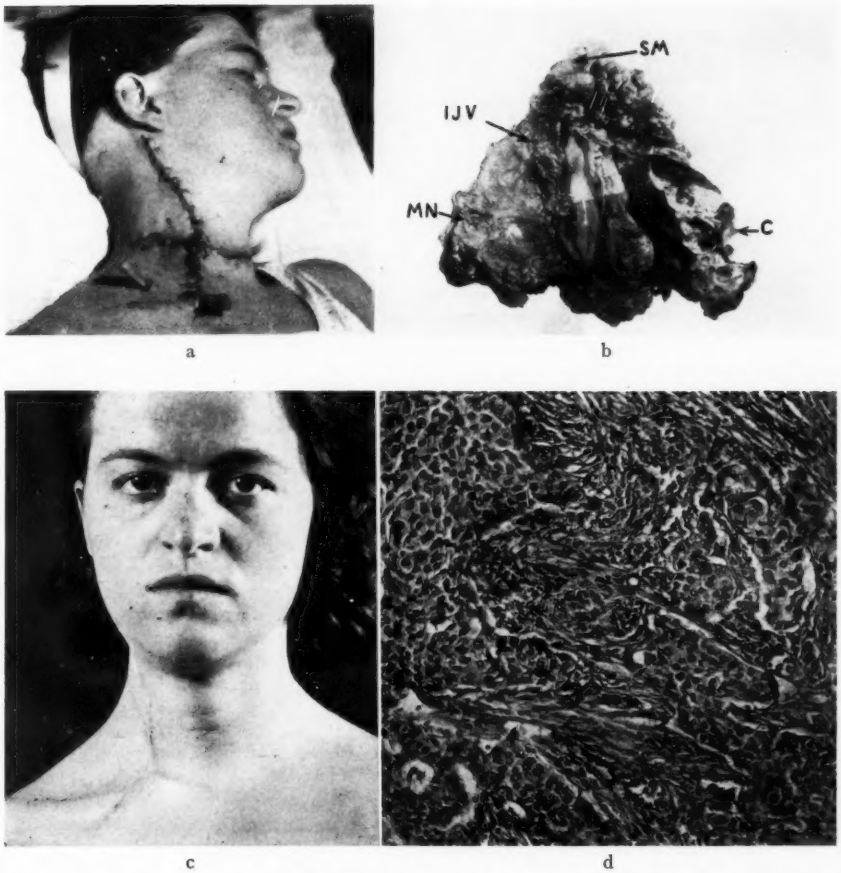



Fig. 17. R. B. a, Immediately after radical thyroidectomy under local anesthesia. b, Specimen removed at operation showing primary cancer, *C;* metastases, *MN;* internal jugular vein, *IJV;* and sternomastoid, *SM;* and prethyroid muscles *en masse.* c, Showing altered contour of the healed neck. d, Papillary adenocarcinoma.

being slightly anterior. The incision was then crossed by a transverse incision extending from the anterior border of the trapezius muscle directly forward, overlying the prominence of the laryngeal cartilage and extending slightly to the left of the midline. The four skin flaps thus made were dissected exposing the neck structures. Exposure revealed chains of metastatic nodes along the superior thyroid vessels, adherent to the internal jugular vein and also extending below the sternum along the course of the lowermost thyroid veins. Another group of nodes was noted in the posterior cervical triangle. The tumor was mobilized by resecting the sternomastoid and the prethyroid muscles. The internal jugular vein was sectioned above its superior thyroid branch and below the inferior branch. The primary tumor, right lobe, and isthmus of thyroid gland, the internal jugular vein, prethyroid and sternomastoid muscles, together with the contents of the posterior cervical and substernal triangles were removed in one mass as shown in Figure 17b. The wound was closed with two large cigarette drains and a bulky pressure dressing was applied.

*Final diagnosis:* carcinoma of the thyroid with metastases to the right neck and substernal lymph nodes.

*Pathological diagnosis:* papillary adenocarcinoma of thyroid, grade 2, metastatic to nodes.

The patient's postoperative course was uneventful. Paralysis of the right side of the tongue with some atrophy and paralysis of the right side of the larynx developed. Her basal metabolism rate about

2 weeks after the operation was minus 13. Her voice and larynx symptoms gradually disappeared and she gained weight. At the time of operation her weight was 145 and at the present time it is 164½. The basal metabolism rate March 30, 1939 was minus 19. Patient is taking 1½ grains of thyroid extract each day (Fig. 17).

### END-RESULTS

In discussing end-results in thyroid cancer, one must necessarily consider "survival" rates rather than "cure" rates, because we know that this disease may recur or metastasize many years after treatment. In the present series 2 cases are included in which fatal thyroid cancer recurred locally 16 years after the original treatment, and one of these patients coming to autopsy had massive metastatic thyroid cancer in the mediastinal lymph nodes, but no cancer in the neck.

As present methods of treatment were not in vogue prior to 1934, little of value is to be derived from a study of the 5 year survivals. However, of the original group of 167 patients, there are 53 living: 4 for 10 years or more, 9 from 5 to 10 years, and 26 less than 5 years—all free of disease.

### SUMMARY

1. A series of 167 cases of carcinoma of the thyroid is examined from both the surgical and radiotherapeutic viewpoints.

2. Papillary adenocarcinoma is the most common form of malignant thyroid lesion.

3. Lymphosarcoma, apparently primary in the thyroid gland, was noted in 5 instances. This lesion proved radiosensitive. Cancer occurred in the lingual thyroid in 3 cases.

4. Thyroid cancer cannot be classed as a radiosensitive type of new-growth. It responds best to a combination of surgery and interstitial radiation in the form of gold filtered radon seeds.

5. A pre-operative diagnosis of thyroid cancer was confirmed by aspiration biopsy in 83 per cent of the 74 cases in which it was employed.

6. An operation designed to remove a malignant thyroid lesion together with the major cervical veins and lymph nodes of the affected side is described. There was no operative mortality in the small series in which this procedure was carried out.

7. Fifty-three patients of the original 167 are living and 4 are free of disease 10 years or more, 9 for more than 5 years, and 26 for less than 5 years.

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# CLINICAL SURGERY

*FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF TEXAS*

## SPLENECTOMY

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THE mortality following splenectomy was given by W. J. Mayo in 1928 as 10 per cent and by Pemberton as 6.7 per cent. Eliason and Ferguson give it as 13.7 per cent in all cases and 34 per cent in the acutely ill. The complications commonly recorded as associated with splenectomy are hemorrhage, thrombosis of the portal circulation, disruption of the abdominal wound, and injury to the diaphragm and pancreas.

Temporary occlusion of the splenic artery preliminary to splenectomy has been advised by Miller, Cutler, and others, while permanent occlusion has been more often used. Ligation alone as a substitute for splenectomy in extreme cases has been practiced extensively by Alessandri and others. Obviously, splenectomy is preferable because ligation of the artery reduces the blood supply to the spleen only temporarily.

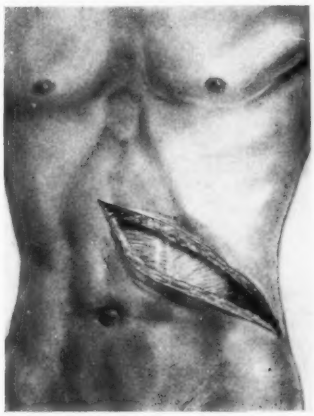
The indications for splenectomy, the pre-operative preparation, and the postoperative care should be given serious consideration. Postoperative thrombosis of the portal system is an acknowledged danger about which little can be done, but the loss of blood at or following operation is the most serious complication one has to anticipate. My respect for this complication dates back to the first splenectomy I ever witnessed during my medical school days. Though an excellent surgeon was operating upon a difficult spleen, veins were torn and a fatal hemorrhage resulted.

We offer a technique for splenectomy which has served us well, the chief advantage of which is an incision that gives adequate exposure and allows the surgeon complete control of the situation even in cases in which the liver, as well as the spleen, is greatly enlarged.

The patient is tilted slightly to the right side. The skin incision is begun at the midepigastric line, half way between the ensiform and umbilicus, and is extended laterally and downward to just above the crest of the ilium, which is in the line of the fibers of the internal oblique muscles. The anterior sheath of the rectus muscle is incised and the incision is carried across the fibers of the external oblique fascia to where it becomes muscular. The rectus sheath is dissected off its muscle upward and downward for a short distance and the muscle is retracted medially. This exposes the posterior sheath which is incised across from the linea alba outward and downward and between the fibers of the internal oblique. The transverse muscle is cut in the same line without separating it from the internal oblique. The tenth intercostal nerve is retracted with the rectus muscle, while the eleventh nerve is cut and the twelfth is retracted laterally.

The use of a gastric suction tube put in place before the anesthetic is started, to collapse the stomach, gives greater room, and if it is retained for 24 to 48 hours it lessens the danger of displacing ligatures off the greater curvature of the stomach and also results in a smoother convalescence.

The ligation of the splenic artery is an important second step. In the very obese the vessel may not be visible, but its pulsation will be felt



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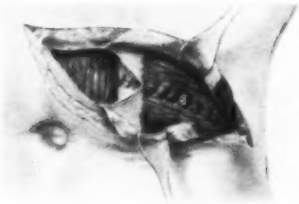

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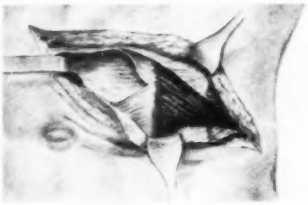

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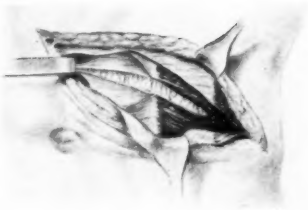


Fig. 4.

Fig. 5.

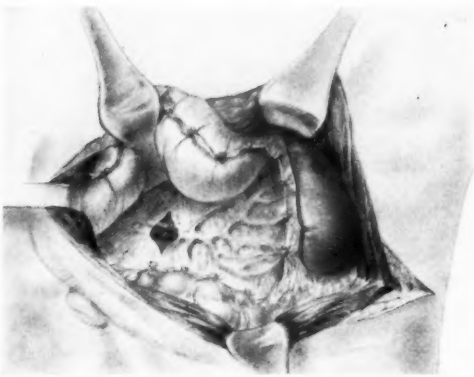
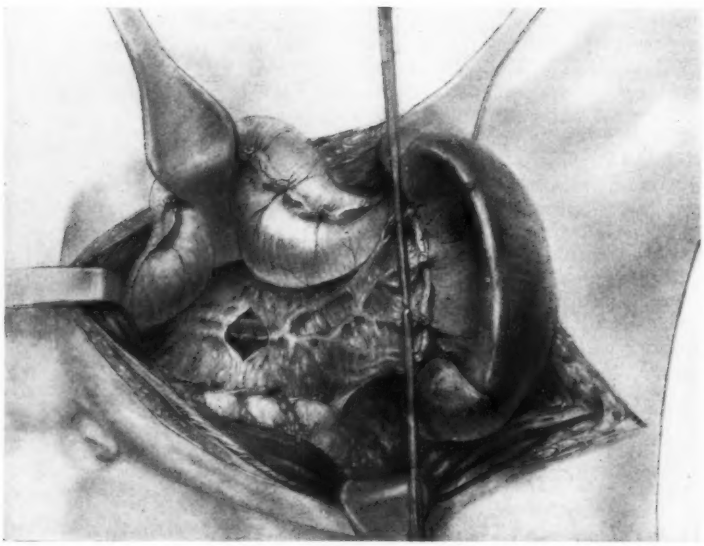


Fig. 6.



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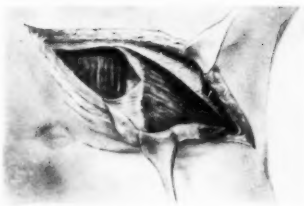

Fig. 8.

Fig. 9.

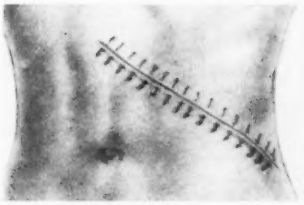

Fig. 10.

along the upper border of the pancreas when the lesser peritoneal cavity is opened. Care should be taken not to tear or include the splenic vein in the ligature. Almost immediately the spleen will reduce in size, thus making the gastrosplenic vessels accessible for severing between ligatures placed well away from the stomach. The separation of the spleen from the splenic flexure of the colon and upper pole of the kidney is next done, with careful ligation of all structures severed. Only now should the spleen be delivered out of the abdomen. After the spleen has been freed of its attachment to the diaphragm, the remaining hilus structures are clamped and then ligated. Following removal of the spleen, there is good exposure of the diaphragm and oozing vessels may be clamped and tied or coagulated with the radiocautery. Thus a dry bed is left and the necessity of packing with gauze is obviated. A continuous stitch sutures the posterior rectus sheath and the transverse and internal oblique muscles with the peritoneum. A second suture closes the anterior rectus sheath and external oblique fascia. A strong abdominal wall results.

The incision is unanatomical in that the fascia of the external oblique, as well as of the transverse muscle, is cut across its fibers. The injury to the intercostal nerve leaves no permanent evidence of damage, either to sensation or to muscle control.

# THE REPAIR OF INGUINAL HERNIA

## A Standardized Technique

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THE purpose of this paper is to review certain factors regarding the diagnosis and treatment of inguinal hernia and to present a standardized technique which we have successfully used in a large series of cases.

Almost all present day operations for the repair of inguinal hernia, direct or indirect, are modifications of the Bassini or Halsted technique. Bassini first devised his method of repair in 1884 and Halsted (3) his in 1888. The use of fascia in operations for hernia was first reported by McArthur in 1901. He utilized strips of fascia derived from the aponeurosis of the external oblique in conjunction with the Bassini method of repair. Ferguson was the first to place the cord external to the aponeurosis of the external oblique. His method of repair was published in 1899. Kirschner, in 1910, reported 40 successful operations in which he used a free flap of fascia lata secured by separate incisions in the thigh and sutured ventral to the conjoined tendon.

*The anatomic basis.* In its migration from the lumbar region of the abdomen into the scrotum, the testicle is preceded by a portion of the peritoneum, the processus vaginalis, which normally becomes obliterated shortly after birth. The various types of indirect hernia which develop will depend upon the amount and degree of obliteration of this funicular process. The sac comes obliquely through the abdominal wall by virtue of its close association with the spermatic cord structures. An indirect hernia is therefore considered to be of congenital origin.

Zimmerman states that the conviction grows that the underlying predisposing anatomical basis for direct hernia consists of a congenital absence of adequate muscular support for the lower portion of the inguinal canal. He believes that this further explains the fact that most men go through life doing hard labor and do not develop direct hernias whereas others, who are relatively inactive, have direct hernias before middle life is reached. Although direct hernias are considered to be acquired, attempts have been made to explain them on a congenital basis as well.

*Differential diagnosis.* Since the sac of a direct hernia pushes its way through the abdominal wall in an area known as Hesselbach's triangle, the tip of the examining finger when inserted through the external inguinal ring will appear to pass directly into the pelvic cavity. The floor of Hesselbach's triangle is formed by the transversalis fascia, the base by Poupart's ligament and the superior ramus of the pubis, the lateral boundary by the deep inferior epigastric artery, and the medial boundary by the lateral portion of the straight muscle of the abdomen and its sheath. If a firm resistance is felt by the examining finger in Hesselbach's triangle and an impulse is palpated in association with the cord structures, the diagnosis of an indirect hernia can be made. The patient should be examined in both the erect and recumbent positions. Very little pain is associated with direct inguinal hernias and they seldom become incarcerated because of the wide mouth of the sac and the direct course which the sac follows from the abdomen. The sac of a direct hernia does not enter the scrotum because there is no connection with the spermatic cord structures. In certain cases in which a double, saddlebag, or pantaloon type of hernia is present, the accurate pre-operative differentiation may be difficult. The fact that bilateral inguinal hernia is present is of no significance in diagnosis since either type may be bilateral.

When a direct hernia is found at operation, a careful search should be made of the cord structures at the internal inguinal ring for the presence of an indirect sac or of a pantaloon type of hernia. Failure to examine the cord structures carefully accounts for a small number of recurrences, which are, in fact, hernias overlooked at the first operation.

### TECHNIQUE OF OPERATION

An average of 410 inguinal hernia operations are performed each year at Hines Hospital. Because of this large number of cases, a satisfactory uniform technique has been devised and used by one of us (P. F. B.) for many years. Although the

Read at a meeting of the Army-Navy Medico-Military Symposium, Rochester, Minnesota, October 11, 1939.

From the Surgical Service, Edward Hines Jr. Hospital, Hines, Illinois.

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follow-up system has not been 100 per cent in all cases, the number of recurrences is considered to be less than 3 per cent for both the direct and indirect types. The majority of the patients live in the vicinity of Hines Hospital and return voluntarily for follow-up or for other conditions, which provides an opportunity for check-up. Since the results have been so successful over a period of years in a large series of cases, we believe a description of the operative technique is worth reporting.

Spinal anesthesia is used wherever possible. If a bilateral inguinal hernia is present, 200 milligrams of procaine is inserted intraspinally between the second and third lumbar vertebræ; if a single hernia is present, 150 milligrams of procaine is used (8). In addition to preparation of the operative site with an antiseptic solution, a piece of gauze saturated with the solution is placed about the penis and scrotum to prevent infection. The pubic spine and cord structures are carefully palpated and the incision is made obliquely upward midway between the rectus border and Poupart's ligament (Fig. 2). If necessary, the incision is extended over the pubic spine. The fibers of the external oblique aponeurosis are incised above the level of the internal inguinal ring and the flaps are reflected to either side. The ilioinguinal nerve is placed aside in order not to damage it. The spermatic cord structures are opened near the internal inguinal ring so that a careful search can be made for the presence of a hernial sac. A sac of the indirect type can then be separated from the cord structures which are held out of the field of operation by means of a piece of cord tape. The cremasteric muscle and fat are dissected free of the cord. The sac is carefully dissected free down to its neck, opened, and its contents replaced within the abdomen, drawn together by purse-string sutures at its neck, and excised (Fig. 1). The stump of the sac is allowed to retract normally and it is not sutured beneath the internal oblique muscle or to any structure. In those cases in which the ligated sac is sutured to the internal oblique muscle it is believed that a potential hernia is created because of the pull on the peritoneum. The floor of the inguinal canal is dissected free of all cremasteric muscle, fat, and all vascular structures which might interfere with proper closure. If a small direct hernia is present, the sac is not incised, but it is reduced and invaginated by means of interrupted sutures in the transversalis fascia which cover over the bulging defect and invaginate the redundant tissue (Fig. 3). If the direct hernia is large, it is incised, the redundant sac is excised, and the procedure just described is carried out

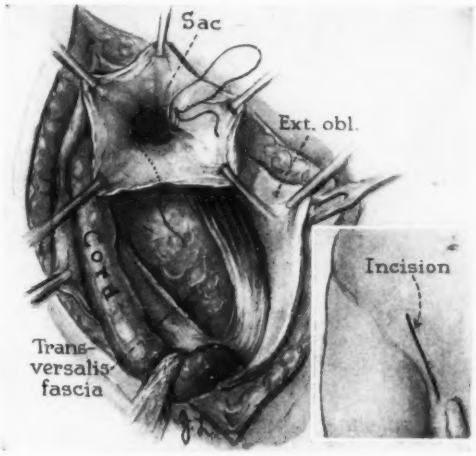


Fig. 1




Fig. 2

after closure of the base of the sac. The remainder of the repair is the same for either direct or indirect inguinal hernia.

Since the great majority of recurrences develop at or near the pubic bone, the first suture is placed through the periosteal fascial covering of the pubic spine, the conjoined tendon, and the shelving edge of Poupart's ligament. A number of interrupted sutures are taken from this point up to the internal inguinal ring. They approximate the conjoined tendon and the internal oblique to the shelving edge of Poupart's ligament. The angle of the cord structures is changed at the internal inguinal ring by retraction of these structures upward and by placing sutures close to the cord. Two interrupted sutures are also taken above the internal inguinal ring (Fig. 4). The lateral flap of the external oblique is then sutured medially beneath the cord to the fascia of the internal oblique and conjoined tendon by means of interrupted sutures (Fig. 6). The cord is thus turned medially on the internal oblique by the overlapping lateral flap at the internal inguinal ring for a distance of approximately 1.5 centimeters. Additional sutures are taken above the cord to strengthen this area. The medial flap of the external oblique is incised for about 1.5 to 2 centimeters opposite the cord structures at the level of the internal inguinal ring (Fig. 5). The cut edges are then sutured laterally about the cord. The remainder of the medial flap of the external oblique is sutured laterally beneath the cord to the external oblique fascia by interrupted sutures (Fig. 7). Suture of the lateral flap of the external oblique medially over the cord at its exit

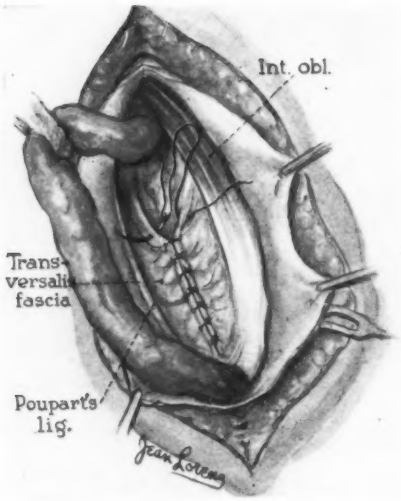


Fig. 3

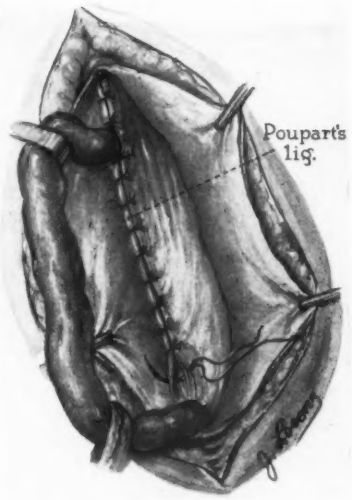


Fig. 4

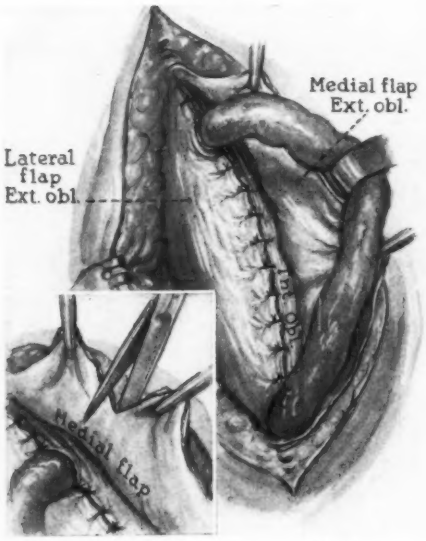


Fig. 5

Fig. 6

Fig. 7

from the internal inguinal ring and then suture of the cut edges of the medial flap of the external oblique laterally about the cord not only change the direction of the cord but make a new internal inguinal ring. A recurrence at this point is therefore quite difficult. The cord structures are transposed between the superficial fascia and the external oblique aponeurosis. We have had no complications at the internal inguinal ring from the use of this method.

The conjoined tendon consists of those parts of the internal oblique and the transversalis muscles which unite to insert into the pubic bone (crest and tubercle) in front of the straight muscle of the abdomen. Many variations, however, are found

in the way these two structures form the conjoined tendon. The conjoined tendon therefore may be almost completely muscular or completely fascio-aponeurotic. We do not hesitate to suture the internal oblique muscle to the shelving edge of Poupart's ligament. If the muscle is traumatized a firm union will result. Although Seelig and Chauke are of the opinion that muscle sutured to fascia does not unite with it but simply forms an adhesion which becomes weakened under pressure, we believe that such union is adequate provided the flaps of the incised external oblique have been sutured over to make a double layer. Russell believes that suture of muscle injures it, prevents its action, and predisposes to recurrence. He also believes that proper removal of the sac alone is sufficient in the cure of simple indirect inguinal hernia. We have had occasion to operate upon patients for recurrent hernia in whom muscle was sutured to fascia and have found a firm union to be present. The removal of the indirect sac and reapproximation of the tissues may be sufficient in children but will prove to be highly unsuccessful in adults.

### PRE-OPERATIVE AND POSTOPERATIVE CARE

The patients are hospitalized at least one day prior to operation and are given a complete physical examination, including routine laboratory tests. A soap suds enema is given on the night before operation and on the morning of operation. Just before the patient is taken to the operating room he is given ¼ grain of morphine preliminary to the spinal anesthetic.

After operation the patient is placed in a moderately flexed position by elevating the head of the bed (24 hours after operation) and raising the knees. This provides more comfort for the patient and relaxes the tension on the wound. The patient is kept in bed for 14 days and is advised not to do any heavy work for at least 2 months. If he is obese, a reducing diet is advised prior to and following the operation. No abdominal supports of any type are prescribed for use following operation. Gas pains are readily relieved by the insertion of a rectal tube and by the administration of prostigmine.

### EVALUATION

In the past 2000 inguinal hernia repairs, fascial grafts or sutures have not been used in the treatment of more than 3 patients. We believe that if the technique described herewith is carefully executed and the patient is kept in bed for a period of 14 days following operation, there is little need for fascial grafts. Either silk or chromic catgut sutures may be used. In the majority of the patients in this series, chromic No. 1 catgut was used.

Articles have appeared in which it is stated that the risk of complications in operations for bilateral inguinal hernia is nearly twice that of single hernia; also that wound infections occurred more than twice as often in cases of bilateral hernia. This has not been our experience.

We have had no occasion to use the injection method of hernia treatment, with such solutions as sylnasol, monolate, proliferol, or neogaltanol. It has been noted, however, in the patients upon whom we have operated who had been given the injection treatment, that the hernias were still present and that the fibrosis produced interfered with the normal tissue planes and made surgical repair more difficult.

### SUMMARY

A standardized technique for the repair of inguinal hernia which has been successfully used in an average of 410 patients annually over a period of years is reported. The recurrences number less than 3 per cent. Fascial grafts are not used. Pertinent facts regarding the diagnosis and treatment of inguinal hernia are also reviewed.

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# PERIPHERAL VASCULAR DISEASE

## A Critical Survey of Its Conservative and Radical Treatment

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New Orleans, Louisiana

EFFECTIVE therapeusis in peripheral vascular disease, as in other conditions, is necessarily dependent upon rational considerations of the physiopathological alterations. These changes and their reflected manifestations in peripheral vascular diseases are simply due to a disturbance or actual diminution in the normal amount of circulating blood to a part and are usually the result of a varying diminution in the normal caliber of the peripheral vessels. This decrease in intraluminary volume may be caused by obliterative structural change, by abnormal spasticity, or by both, depending upon the type and stage of the disease.

Improvement in circulation is essential for successful therapy and is based upon increasing the blood supply to the part. Obviously this cannot be accomplished by an attack upon vessels which have already undergone structural change. On the other hand, vasospasm is not an unalterable pathological lesion, but a physiological or functional derangement which can be satisfactorily influenced by appropriate therapy. Such a rational conception of peripheral vascular disease forms the basis of the classification which we previously described (61, 62), that is, (1) vasospastic functional disease, (2) vasospastic organic disease, and (3) degenerative organic disease. It becomes perfectly obvious that vasospasm is of decisive importance because it is *the one controllable factor* and therefore of prognostic and therapeutic significance. However, it should be realized that whereas vasospasm may be the predominant feature in certain types of cases in which there is little or no structural vascular change, it exists also in those conditions in which organic vessel disease is the prominent factor. In the latter group vasospasm involves the collateral vessels. Thus, because the degree of vasospasm varies in any given case of peripheral vascular disease, it is necessary to determine not only its presence or absence but also its extent.

In previous publications (61, 62), the authors have reviewed and critically analyzed the various diagnostic procedures which may be employed for the study of and the determination of this phenomenon. Such a survey is beyond the scope of this presentation and the reader who is interested in this phase of the subject is referred to these publications. *It should be emphasized, however, that without the determination of the presence or absence of vasospasm and its extent, rational therapy cannot be applied.* As previously reported, there are certain clinical factors which indicate the presence or the absence of, and in some instances influence, vasospasm. These may be grouped as (A) Indicative factors, under which may be classified age, sex, color changes, pulsation, and hyperhidrosis; and (B) influential factors, which include emotion, environment, and tobacco.

Because peripheral vascular disease consists of diminution in blood supply to the extremities, therapeusis consists of measures aimed to improve the peripheral circulation and may be divided into two large groups: (1) conservative measures and (2) radical procedures. Generally, conservative measures are indicated in all cases of peripheral vascular disease except in the acute vascular catastrophes and in the rapidly progressive peripheral vascular disturbances. In those instances, however, in which the conservative measures fail, more radical measures may become necessary. The conservative measures consist largely of two groups: (1) those which are directed toward the elimination of all factors which increase vasospasm and (2) those factors which produce vasodilatation. Both are equally important, although on the basis of our experience we are convinced that the elimination of the vasospastic factors is of relatively greater importance because the attempts at vasodilatation are likely to be futile if vasospastic influences are still operative. It is surprising how frequently physicians will attempt to produce vasodilatation in patients with peripheral vascular disease and pay little or no attention to the elimination of vasospastic factors. Simple elimination of these factors frequently will be all that is necessary to restore a normal circulation in the extremities.

The vasospastic factors which are of importance are: (1) emotional disturbances, (2) environment, and (3) tobacco. These factors are particularly

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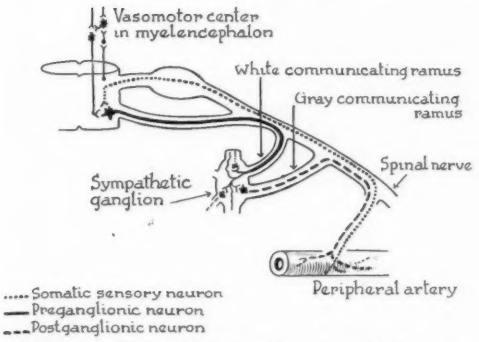


Fig. 1. Diagrammatic illustration of vascular innervation showing pathways of vasoconstrictor impulses, the interruption of which forms the rational basis for sympathectomy.

important in those peripheral vascular diseases associated with a predominance of vasospasm, namely, the vasospastic functional disease and the vasospastic organic disease, and of less importance in those conditions in which there is little or no vasospasm, such as degenerative organic disease. The control of emotions is frequently difficult but every effort should be made to eliminate those factors which incite such emotions as fear, anger, and worry. Physiological disturbances that occur during periods of endocrine disturbance, such as menopause and menstruation, are also of importance and should be corrected as much as possible.

Environment is of great importance in the production of vasospasm. Although it may be difficult for patients to change environment, it is extremely desirable when such is possible. Although commonly the patient cannot move to a warmer climate and thus avoid the vasospastic influence of exposure to cold, such an individual should take particular care to protect the exposed portions of his body from cold at all times. The wearing of woolen stockings, the protection of the hands and arms with long gloves, the avoidance of contact with cold water, of dampness to the feet, and the necessity of wearing bed socks cannot be overemphasized. Far too frequently, a young girl with a vasospastic functional disease that involves the upper extremities may be warned about the care of her hands and arms but may not be given adequate instructions concerning the protection of her lower extremities and will be allowed to saunter forth in the cold with her ankles and calves protected only by the sheerest silk. In such an instance, the reflex vasospasm of the involved extremities is almost as great as direct exposure of the extremity itself to cold.

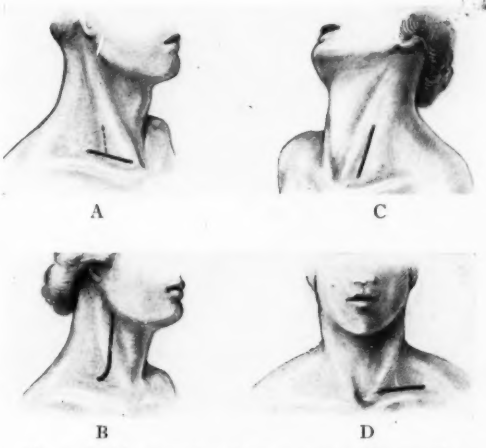


Fig. 2. Incisions employed for cervicodorsal sympathectomy by anterior approach. A, Inverted T-shaped incision of Royle, 1924 (73). The dotted vertical bar is optional. B, Hockey stick incision of Davis and Kanavel, 1926, used for resection of the entire cervical chain. C, Longitudinal incision between two heads of sternocleidomastoid muscle described by Leriche, 1926 (47, 48). D, Transverse incision of Gask, 1933.

Tobacco smoking is indubitably one of the most important precipitating factors in vasospastic conditions, not because it exerts a more drastic inherent influence than environment and emotion, but because it is more frequently disregarded and is not constantly present. We are so convinced of the vasospastic influence of tobacco that we believe that it is impossible for a patient with a peripheral vascular disease associated with vasospasm to recover as long as there is indulgence in smoking. The definite deleterious effect of smoking upon the vascular system has been shown repeatedly. Numerous investigators have revealed that tobacco produces a marked vasoconstriction of the peripheral vessels in normal individuals as well as in patients with vascular disease. Although some investigators believe that there exists a hypersensitivity to tobacco which is particularly marked in vasospastic organic diseases, others have not been able to confirm these findings. Whereas smoking may be injurious to patients with organic degenerative disease because of the vasospastic influence upon the collaterals, it is especially harmful in patients with vasospastic functional and vasospastic organic lesions.

In addition to the elimination of the vasospastic factors, which as just mentioned is all important, in many instances it is desirable to produce vasodilatation which may be done in one of the fol-

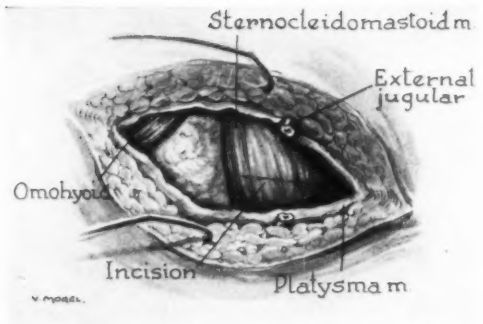


Fig. 3. Cervicodorsal sympathectomy by anterior approach as preferred by the authors. After a transverse incision as shown in Figure 2, D, is made, the clavicular head of the sternocleidomastoid muscle is either severed or retracted medially and the omohyoid is retracted upward.

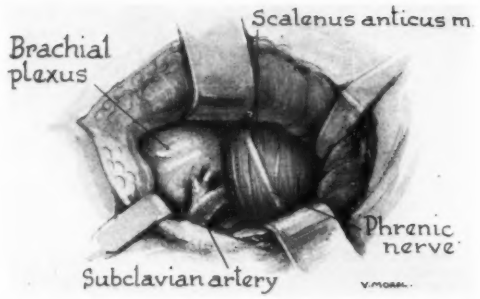


Fig. 4. Exposure of the anterior scalene muscle and the phrenic nerve lying over it is readily accomplished after dissection of the loose areolar fascia has been done. The phrenic nerve should be carefully retracted before division of the anterior scalene muscle is carried out.

lowing different ways: (1) application of heat, (2) drugs, and (3) vascular exercises. It is well known that the application of heat to a part will produce normally an increased vascularity. Because of the diminished blood supply to an extremity in a peripheral vascular disease and the resultant inability to carry away an excessive amount of heat applied to such an extremity, the application of heat to the involved extremity is not without danger and should not be used at all or with extreme caution. The application of heat to the involved extremity is not necessary because, as shown by Lewis and Pickering (54, 67) and emphasized by Gibbon and Landis (32, 42, 43), application of heat to a localized portion of the body produces a generalized vasodilatation. Thus, equally as good results can be obtained by the application of heat to an uninvolved extremity without the danger of injury to the involved extremity by the heat applied directly to it. A patient with vascular disease of the lower extremity should immerse his hands and arms for 20 to 30 minutes, two to three times a day and, similarly, a patient with a peripheral vascular disease that involves the upper extremity and is associated with vasospasm should immerse the lower part of the body in hot water for 20 to 30 minutes, two or three times a day.

Many drugs have been used in the production of vasodilatation. Probably one of the most widely employed and yet one of the most efficacious is alcohol. Generally, we advise these patients to take one or two highballs daily, preferably, in the case of the business man, before dinner in the evening and just before retiring at night as this will interfere less with his daily routine. Carbaminylcholine or acetyl-beta-methylcholine chloride (mecholyl) is also an efficient vasodilatating substance and is of value in the conservative treatment of peripheral vascular disease associated with vasospasm. It may be administered orally, hypodermically, intra-arterially, or by iontophoresis. Of the various methods, the subcutaneous administration is probably the most efficacious but has the limitation of requiring a hypodermic injection. Papaverine hydrochloride has also been widely employed especially in acute peripheral vascular catastrophes. More recently, however, it has been shown to be a less effective vasodilator than the simple water immersion procedure. Other drugs advocated are theobromine, sodium thiosulphate, and sodium iodide. Theobromine has been found to be of little value in the treatment of peripheral vascular disease and the others are also considered of dubious value. More recently the authors have employed a new drug, beta-dimethyl-amino-a phenyl-a-aethyl-propionic acid benzyl-ester hydrochloride (DL 219), with more promising spasmolytic effects. Histamine administered by iontophoresis has been used by some investigators with reportedly good results. Pancreatic tissue extract and muscle tissue extract have also been advocated as vasodilator agents. More recently prostigmine and testosterone propionate have also been suggested.

Vascular exercises are of value in some cases of peripheral vascular disease. Buerger originally described the exercises known by his name and found that when systematically used they were of distinct benefit in the promotion of collateral development. Probably of more value than the Buerger exercises are those exercises obtained by

means of a tilting bed. This is particularly true in patients who have progressive lesions and who are confined to bed. Passive vascular exercises by mechanical devices have been used extensively in the treatment of peripheral vascular disease. This form of therapy probably is of greatest relative value in those patients with degenerative organic disease because they have little or no associated spasm. Veal (80, 81) has shown, however, that in those instances in which this method of therapy may be beneficial in patients with extensive collateral circulation, it is of little or no value in those patients who have marked diminution of the vascular bed. Obviously the method has distinct limitations because these patients are in greater need of circulatory improvement. Kountz (39, 40) found that little benefit is derived from the use of this machine and deTakats (21) and Veal (81) believe that the degree of involvement present at the onset of treatment is the most important factor in the determination of the degree of benefit which may be obtained by this form of therapy.

Based upon the original observations of Bier (10), Moszkowicz and Matas, and the extensive studies of Lewis and his co-workers (7, 8, 53, 55, 68) on the principle of reactive hyperemia, intermittent venous occlusion has been developed as a simpler and less expensive method of therapy than passive vascular exercises. Here again, the limitations of this form of therapy are much the same as for the passive vascular exercises. DeTakats (20) found that it had no beneficial influence on pure vasospastic functional disturbances and its limited value has also been indicated by others.

Whereas many of these conservative measures are justified and are usually sufficient to produce complete relief of symptoms, in the rapidly progressive case and especially in the case associated with a prominent degree of vasospasm, attack upon the sympathetic nervous system is considered desirable. The concept that in these vasospastic states sufficient vasoconstrictor impulses are transmitted over the sympathetic pathways to cause diminished circulation and that the release of these impulses may be enough to permit the return of circulation to normal, forms the rational basis for sympathectomy (Fig. 1). Interruption of impulses over sympathetic pathways may be accomplished by chemical block or by resection. A chemical block may be done temporarily by the injection of procaine hydrochloride into the appropriate ganglia, or for a longer period of time by the use of alcohol. *Whereas it may appear that block of the regional sympathetic ganglia in peripheral vascular disease is more radical than the use of vascular exercises, actually it is a more conservative procedure because the patient is completely relieved within a period of a few minutes and thus obviates the expense and loss of time required by the prolonged therapy of vascular exercises.*

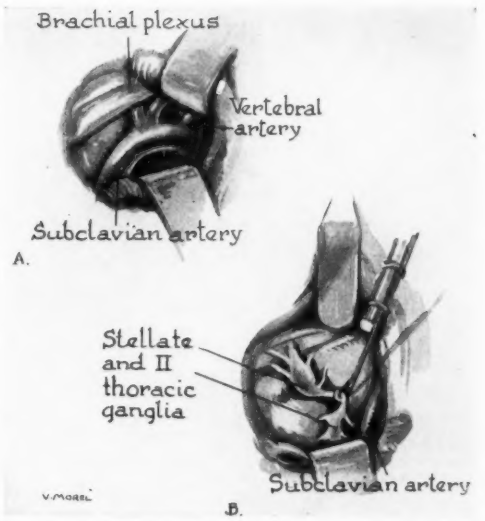


Fig. 5. A, Adequate exposure is readily obtained by severance of the tendinous insertion of the anterior scalene muscle. The subclavian artery and its branches, the thyrocervical trunk and vertebræ, are then easily identified. Occasionally it may be necessary to ligate and sever the inferior thyroid artery. B, The vertebral artery is retracted medially and the subclavian inferiorly to permit exposure of the stellate ganglion lying just behind the junction of these vessels and directly against the anterolateral aspect of the bodies of the vertebræ. A blunt hook attached to a light is used to hold the ganglion while its rami are freed from the surrounding loose fascia. By mobilizing Sibson's fascia and retracting the dome of the pleura downward, the thoracic trunk can be easily followed as far down as the third or fourth thoracic ganglion.

As previously emphasized (61, 62), an alcohol block of the sympathetics should never be done except following a procaine hydrochloride block. The diagnostic significance of this procedure was first championed by Leriche (45, 50), in 1927, and has since been popularized by others. The procedure of the injection of the paravertebral sympathetic ganglia with procaine hydrochloride can be performed with relative facility and safety. The technique has been described previously by the authors (63). Usually the injections are done in the outpatient clinic, since there is no necessity of admission to the hospital for the performance of this procedure. After the insertion of the needles into the appropriate sites, 5 cubic centimeters of

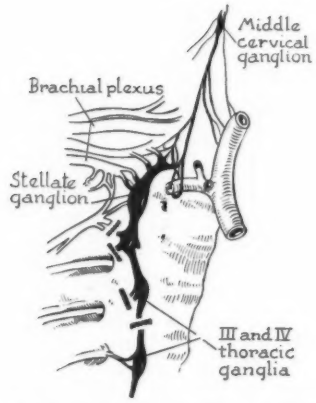


Fig. 6. Diagrammatic illustration of preganglionic sympathectomy as performed by Telford (78). The rami of the second and third dorsal ganglia and the trunk below the third dorsal ganglion are sectioned.

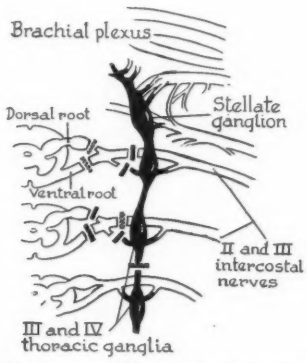


Fig. 8. Diagrammatic illustration of preganglionic sympathectomy described by Smithwick (75). The procedure consists essentially of dissection of the second and third intercostal nerves into the intervertebral foramen, division of the dural attachments, section of their anterior and posterior roots, and division of the sympathetic trunk below the third dorsal ganglion.

1 per cent procaine hydrochloride is injected through each needle and the needles are allowed to remain in position for approximately 15 minutes. During this time the extremity is carefully watched and appropriate studies are made to determine if the vasodilatory response has been sufficient to justify the injection of alcohol. If vasodilatation occurs, then 5 cubic centimeters of 95 per cent alcohol is injected through each needle and the needles are removed. The patient is allowed to get up in about an hour.

In the presence of marked vasospasm in patients with impending vascular catastrophes or in those patients in whom conservative measures fail to relieve the vascular manifestations, radical therapy is justified. Sympathetic denervation of the affected part, however, should not be performed unless the diagnostic test of procaine hydrochloride block has previously demonstrated a satisfactory response of vasodilatation.

In a previous publication the authors (62) reviewed and critically analyzed the common observation that whereas the immediate results following sympathectomy in vasospastic diseases of both the upper and lower extremities are almost invariably excellent, the end-results in the lower extremities are considerably better than those in the upper. The not infrequent comparative failure of cervicothoracic sympathectomy to maintain chronic vasodilatation was attributed to such factors as regeneration, the existence of a greater physiological activity of the vasomotor nerves in the lower extremities than in the upper, and to incomplete interruption of sympathetic pathways.

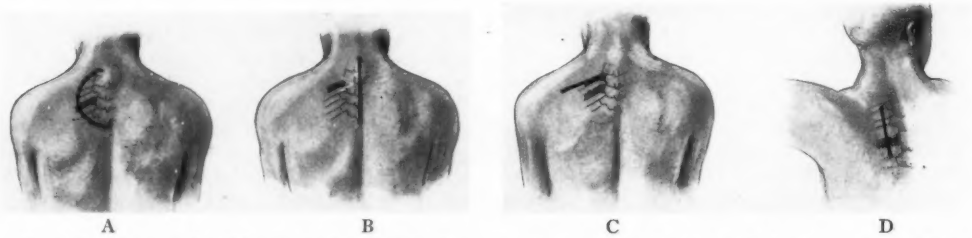


Fig. 7. Incisions employed for cervicodorsal sympathectomy by posterior approach. A, Curved incision described by Henry, 1924. Shaded area of second rib shows portion resected. B, Longitudinal midline incision described by Adson and Brown, 1929 (3, 4). Although resection of portion of second rib was originally advocated in a subsequent description (1), resection of portion of first rib and transverse process as shown by shaded area was considered preferable. C, Oblique muscle splitting incision described by White, Smithwick, Allen, and Mixter, 1933 (86). Either first, second, or both ribs and corresponding transverse processes are resected. D, Vertical paravertebral incision of Smithwick, 1936 (75). Portion of third rib and transverse process are resected as shown by shaded area.

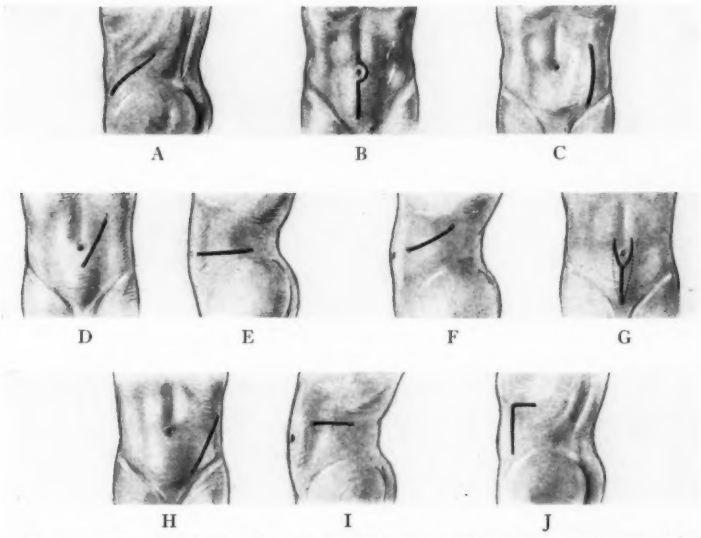


Fig. 9. Approaches for lumbar sympathectomy. A, Extraperitoneal approach by posterolateral incision of Royle, 1924 (70, 71). B, Transperitoneal approach through anterior midline incision described by Diez, 1925, Davis and Kanavel, 1926, and Adson and Brown, 1929. C, Anterolateral extraperitoneal approach described by Leriche, 1926 (46, 49). D, Oblique anterolateral incision described by Pfeiffer and Livingston, 1935 (65, 66) by extraperitoneal approach. E, Transverse incision of Harris, 1935, for extraperitoneal approach. F, Anterolateral oblique incision of Flothow, 1935, for extraperitoneal approach. G, Y-shaped incision of Rees, 1936, for bilateral lumbar sympathectomy by extraperitoneal approach through single incision. H, Oblique anterolateral incision of Pearl, 1937, for extraperitoneal approach. I, Transverse lateral lumbar incision of Leriche, Pereira, and DeBakey, 1937 (51) for extraperitoneal approach to splanchnics and first and second lumbar sympathetic ganglia. J, Inverted L-shaped lateral incision of Smithwick, 1938, for extraperitoneal approach.

The most seriously considered explanation has been that of White, Freeman, and Smithwick (29, 30, 82–84) and Ascroft who directed attention to the significant fact that in contrast to the conventional lumbar sympathetic ganglionectomy, which is actually a preganglionic neurectomy, following the customary procedure of cervicothoracic ganglionectomy for the upper extremity, degeneration of the postganglionic neurons occurs with resultant hypersensitization of the denervated vessels to the circulating hormone, epinephrine. This thesis is based upon the original observations of Meltzer and Meltzer (58, 59), Meltzer and Auer (57), and Elliott, and to more recent investigations which revealed in animals that smooth muscle after sympathetic denervation becomes hypersensitive to epinephrine. On this basis, Smithwick (75) and Telford (78) have described and advocated a technique for cervicodorsal sympathectomy in which the preganglionic fibers are sectioned and the postganglionic fibers are left intact.

However, considerable controversy has since developed concerning the relative merits of preganglionic and postganglionic sympathectomy. White (85) and Smithwick (77) have re-emphasized the importance of resecting only the preganglionic sympathetic fibers and Telford (79) concluded that his results in 25 cases were very gratifying. Learmonth also commented favorably upon this form of sympathectomy. Although deTakats (19) reported eminently satisfactory results following preganglionic sympathectomy, more recently (22, 74) he has expressed the opinion that complete sympathetic denervation shows a smaller number of recurrences. In contrast with the views of White, Smithwick, and Freeman are those of Craig and Horton and Fatherree, Allen, and Adson (25, 26). They contend that the successful results following ganglionectomy in Buerger's disease of the upper extremity and the absence of extreme sensitization to epinephrine following cervicodorsal ganglionectomy for con-

Fig. 10. Anterolateral extraperitoneal approach for lumbar sympathectomy as originally described by Leriche (46, 49). Inset shows the slightly curved incision, with its convexity outward along the anterolateral aspect of the abdomen, that extends from a point just below the costal margin to a point about 3 centimeters medial and inferior to the anterior superior iliac spine. The fibers of the external oblique muscle and aponeurosis are separated in the direction in which they run.

ditions other than vasospastic disease militate against the hypothesis of Freeman, Smithwick, and White. Moreover, Fatherree, Adson, and Allen (26) found that whereas increased sensitivity of digital arteries to epinephrine occurred following both preganglionic and postganglionic section for Raynaud's disease of the hands, the degree of increased sensitivity was about the same in both instances. On the basis of their investigations they concluded that "the problem of unsatisfactory results that occasionally follow operation

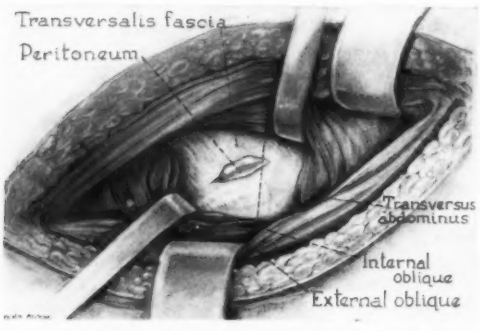


Fig. 12. The authors have found division of the fibers of the internal oblique and transverse muscle of the abdomen unnecessary if good muscular relaxation is obtained by spinal analgesia. Accordingly, these muscle fibers are separated and not severed. The transversalis fascia is thus exposed and incised, care being taken not to incise the parietal peritoneum.

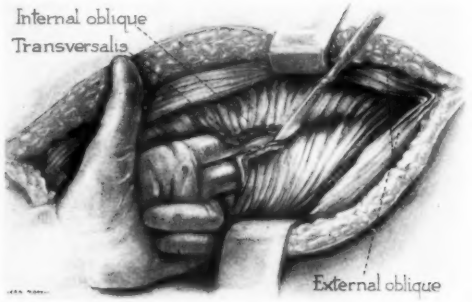


Fig. 11. Anterolateral extraperitoneal approach of Leriche for lumbar sympathectomy showing division of the fibers of the internal oblique and transverse muscle of the abdomen as originally advocated by Leriche.

for Raynaud's disease of the hands has not been satisfactorily solved by a study of sensitivity of digital arterioles to epinephrine." The recent report of Lewis (52) is of particular significance in this regard. He studied 6 patients before and after preganglionic sympathectomy and observed that attacks of discoloration in the fingers occurred spontaneously or were induced in 5 patients within a few days after operation. Although he admits that sympathectomy relieves all patients, it merely lowers the "whole scale of abnormality." However, he contends that it does not remove it, because the attacks are not due primarily "to excessive action of the vasomotor nervous apparatus." He has always maintained that the disease was due primarily to a local fault which may consist either of occlusion, structural disease, or to an increased susceptibility to cold. This is in contrast with the views held by others that sympathetic tone in these patients is abnormally high and that the vasospasm is under a central origin.

Cervicodorsal sympathetic ganglionectomy may be performed by an anterior or a posterior route. It would appear from the literature that the selection of either procedure depends upon personal choice. The authors have employed both approaches and consider the anterior more desirable, because a satisfactory exposure may be obtained with less operative trauma. It is essential, however, in the employment of either approach that the surgeon have an adequate knowledge of the surgical anatomy of this region.

Cervicothoracic ganglionectomy by the anterior approach was originally performed by Jonnesco (36), in 1896, for exophthalmic goiter and epilepsy. However, Alexander, in 1889, is usually credited with having performed the first cervical sympa-

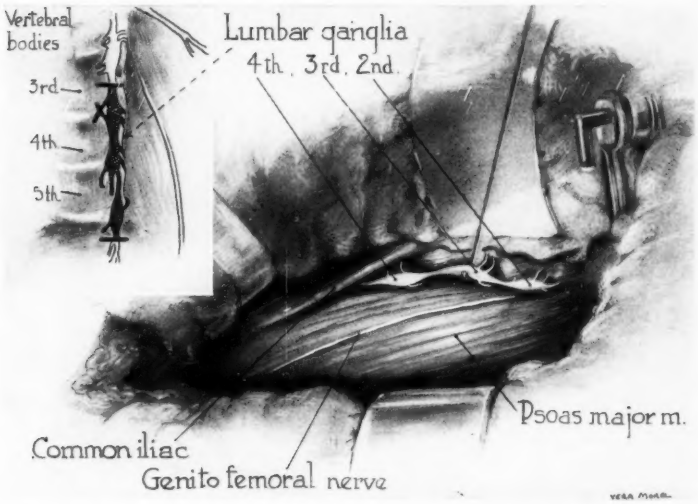


Fig. 13. Anterolateral approach of Leriche for lumbar sympathectomy. By blunt dissection the posterolateral and posterior parietal peritoneum is mobilized medially and held in this position by broad deep retractors. The lumbar sympathetic trunk and ganglia are readily exposed under direct visualization lying between the medial border of the iliopsoas muscle and the anterolateral border of the bodies of the vertebræ. The genitofemoral nerve lying on the anterior aspect of the iliopsoas muscle should not be confused with the lumbar sympathetic chain. Blunt hooks are used to pick up the chain and the rami are freed by careful blunt dissection with small firm gauze tampons applied to the end of long curved forceps. The second, third, and fourth lumbar ganglia and intervening trunk are excised as shown by the shaded area in the inset.

thectomy for epilepsy. Jonnesco (37, 38) subsequently performed the operation for angina pectoris with a brilliantly successful result. Bruening (12, 13), in 1923, appears to have been the first to employ the procedure for vascular disease. He resected the cervicothoracic ganglia for Raynaud's disease and for scleroderma. In 1924, Royle (70, 71) performed sympathetic ramisection by the anterior route for spastic paralysis and in 1927 (72) he advocated the procedure for Raynaud's disease. Whereas in his earlier publications Royle advocated ramisection only, in subsequent presentations (73) he sectioned the trunk below the stellate ganglion. The approach used by Royle consisted of making an inverted T-shaped incision with the horizontal bar in the supraclavicular region and the vertical bar opposite the posterior border of the sternomastoid (Fig. 2, A), reflection of the clavicular attachment of the sternomastoid, and retraction or division of the tendinous insertion of the anterior scalene muscle. Royle stated that the vertical bar of the incision was not always necessary. In 1926, Davis and Kanavel advocated cervicothoracic ganglionectomy for Raynaud's and other vascular diseases and described a somewhat different anterior approach. These authors used an incision resembling a hockey stick which extended from the inferior angle of the mandible downward to the superior border of the clavicle and crossed obliquely the sternomastoid muscle from its medial to its lateral edge (Fig. 2, B). The superior cervical ganglion and chain are exposed by mobilizing the medial edge of the sternocleidomastoid laterally and the middle and inferior cervical ganglia and chain are freed by mobilizing the lateral edge of the muscle medially. Accordingly the superior and middle cervical and stellate ganglia and intervening trunk are resected.

In 1926, Leriche (47, 48) described a much simpler anterior approach which consists of a longitudinal incision about 6 centimeters in length made between the clavicular and sternal heads of the sternocleidomastoid muscle (Fig. 2, C). The dissection is carried down between the two heads of this muscle and the stellate ganglion is exposed medial to the insertion of the anterior scalene muscle. The anterior approach described by Gask (Fig. 2, D) is essentially the same as that previ-

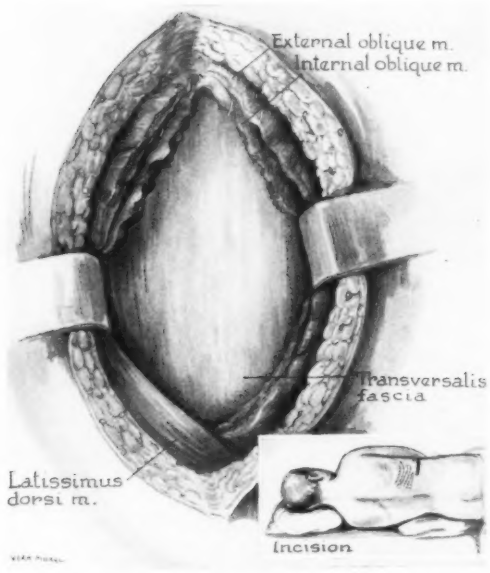


Fig. 14. Extraperitoneal approach of Leriche, Pereira, and DeBakey (51) for resection of splanchnics and first and second lumbar sympathetic ganglia. Inset shows position of patient and the transverse incision which is made just below the costal margin to extend from a point just anterior to the midaxillary line to the lateral border of the sacrospinal muscle. The fibers of the external and internal oblique muscles are separated and incised thus exposing the fibers of the transverse muscle of the abdomen which are separated in the direction in which they run and the transversalis fascia which is incised to expose the peritoneum and retroperitoneal fascia.

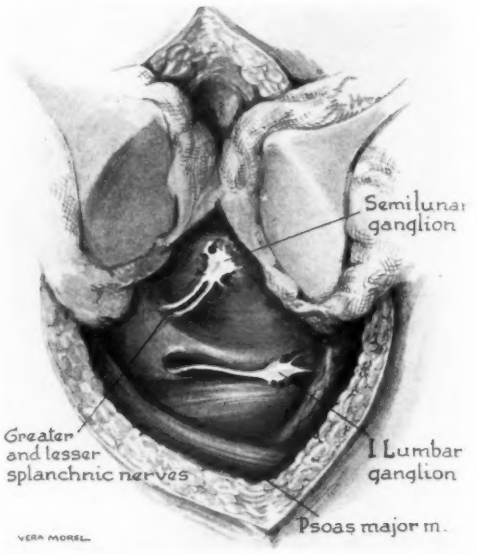


Fig. 15. Continuation of procedure described in Figure 14. The retroperitoneal fascia is gently mobilized forward and held in place by means of deep broad retractors thus exposing the psoas muscle and diaphragmatic crura. The greater and lesser splanchnics are found to emerge from between the diaphragmatic crura and to pass somewhat medially and transversely to enter the semilunar ganglion. The first and second lumbar sympathetic ganglia may be found just below these structures between the anterolateral aspect of the vertebral bodies and the iliopsoas muscle. The splanchnics are severed just before they enter the semilunar ganglion and the first and second lumbar sympathetic ganglia and intervening trunk are resected.

ously described by Royle (70, 73). The authors have found this approach eminently satisfactory. The clavicular head of the sternocleidomastoid muscle is divided and the omohyoid is either retracted or severed (Fig. 3). The anterior scalene muscle is exposed, the phrenic nerve is retracted medially, and the inserting fibers of the muscle are divided (Fig. 4). This is an important step in the operation because adequate exposure is readily obtained by severance of this muscle (Fig. 5, A). The inferior thyroid and vertebral arteries may be easily identified and should be gently retracted toward the midline. A few nerve fibers from the middle cervical ganglion may be observed looping around the inferior thyroid artery. Occasionally it may be necessary to ligate and sever this artery in order to obtain better exposure. On the left side care should be taken not to injure the thoracic duct. An absolutely bloodless field and good illumination considerably facilitate the operation. By gentle retraction of the vertebral artery medially and the subclavian inferiorly the stellate ganglion may be readily identified lying just behind the junction of these vessels directly against the anterolateral aspect of the bodies of the seventh cervical and first thoracic vertebræ. The ganglion varies in size from 1 to 2 centimeters and in appearance from irregularly oval to dumbbell-shaped. It is readily identified by its white, glistening, dense, tough character and by its numerous rami which have given it the stellate description and name (Fig. 5, B). A blunt hook is used to hold the ganglion while its rami are freed from the surrounding loose fascia by gentle blunt dissection with a small firm gauze tampon applied to end of long curved forceps. We devised a lighted hook which facilitates this procedure. After mobilization of Sibson's fascia the dome of the pleura can be retracted downward and the thoracic trunk easily followed to third thoracic ganglion.

Based upon the investigations stated above which tended to show that the customary cervicodorsal sympathectomy was a postganglionic neurectomy and therefore caused degeneration of the postganglionic neurons with consequent hypersensitization of the denervated vessels to circulating adrenalin, Telford (78) has recently described and advocated a technique in which the preganglionic fibers are sectioned and the postganglionic fibers are left intact. He uses an anterior approach and sections the rami of the second and third dorsal ganglia and the trunk below the third ganglion (Fig. 6). On the assumption that the preganglionic components of the first thoracic nerve have no significant function in the sympathetic innervation of the upper extremity, the white communicating ramus of the first thoracic nerve is allowed to remain intact. Kuntz, Alexander, and Furcolo, however, have demonstrated that the preganglionic components of the first thoracic nerve effect synaptic connections with inferior cervical ganglion cells whose axones are relatively widely distributed in the upper extremity. On the basis of these investigations they concluded that in order to produce complete functional sympathetic denervation it is necessary also to interrupt the white communicating ramus of the first thoracic nerve (41).

The posterior approach for cervicothoracic ganglionectomy was originally performed by Henry, in 1922, for angina pectoris (Fig. 7, A). The procedure was subsequently modified by Adson and Brown (3, 4). These authors used a longitudinal midline incision that extended from the tip of the sixth cervical spine to the fourth dorsal spine (Fig. 7, B). Bilateral ganglionectomy may be performed through this incision by a linear division of the trapezius on either side of and parallel with the spinous processes. The spinous attachments of the rhomboid and posterior serratus muscles are divided and the second rib as well as the second transverse process is resected. The parietal pleura is mobilized anteriorly and laterally and the sympathetic trunk exposed. The stellate and second thoracic ganglia and intervening trunk are resected. Because this procedure did not permit adequate exposure of the lower cervical ganglion and resulted in incomplete sympathectomy, Adson (1) subsequently modified the technique and resected the first rib instead of the second.

Because such an operative procedure produces considerable operative trauma to muscle and consequently increases morbidity, White, Smithwick, Allen, and Mixter (86) modified the technique in an attempt to obviate these difficulties. They use a muscle splitting incision somewhat similar to that devised by Head and Bigger for extrapleural thoracoplasty (Fig. 7, C). The proximal 3 centimeters of either the first or second or occasionally both ribs as well as the corresponding transverse processes are resected and the pleura is mobilized as above.

In order to obviate the postganglionic degeneration and the resultant increased sensitivity of the denervated vessels to circulating adrenalin following the customary cervicodorsal ganglionectomy, Smithwick (75) has recently advocated a procedure which utilizes the posterior muscle splitting approach. It consists essentially of resection of a small portion of the third rib and transverse process, dissection of the second and third intercostal nerves into the intervertebral foramen, division of the dural attachments, section of their anterior and posterior roots, and division of the sympathetic trunk below the third dorsal ganglion (Figs. 7, D, and 8). Because in this procedure also the white communicating ramus of the first thoracic nerve is allowed to remain intact, the exception taken by Kuntz, Alexander, and Furcolo to Telford's procedure as herein stated is applicable to Smithwick's procedure.

Lumbar sympathectomy may be performed either by the transperitoneal or the extraperitoneal approaches. The former route has the advantage of permitting bilateral ganglionectomy through the same operative wound. On the other hand, the latter procedure has the advantages of not invading the peritoneal cavity, absence of trauma to the intestines, and a more satisfactory postoperative course. In the authors' hands this has been the procedure of choice.

Lumbar sympathectomy by the transperitoneal approach was first performed for vascular insufficiency of the lower extremities in 1924, by Diez (Fig. 9, B). This author advocated resection of the lumbosacral cord, i.e., the excision of the sympathetic chain and ganglia from the second lumbar to the third sacral, inclusive. Whereas Adson and Brown (3) performed transperitoneal sympathetic ganglionectomy for spastic paralysis in 1924, they (2) first used this operative procedure for vascular disease (Raynaud's) in 1925. However, they resected only the second, third, and fourth lumbar ganglia and intervening trunk. The technical description of this procedure was first presented by Davis and Kanavel, in 1926, and subsequently by Adson and Brown (3), in 1929. The technique consists of making a midline or paramedian incision that extends from a point 5 to 6 centimeters above the umbilicus to a similar distance below (Fig. 9, B). The posterior peritoneal wall is exposed by placing the patient in the

Trendelenburg position and packing the intestines upward and laterally. The chain is exposed by incision of the parietal peritoneum longitudinally along the medial edge of the iliopsoas muscle. On the right side the vena cava is retracted gently and the sympathetic trunk is found lying along the anterolateral border of the bodies of the lumbar vertebræ. Excision of the ganglia and trunk is slightly more difficult on this side because of the lumbar veins which not infrequently pass anterior to the chain. Adson and Brown prefer exposure of the left trunk by incision of the peritoneum along the anterolateral border of the sigmoid and mobilization of this structure medially.

The extraperitoneal approach to the lumbar sympathetic ganglia was originally described, in 1924, by Royle (70, 71) who performed ramisection of the second, third, and fourth lumbar ganglia and section of the trunk below the fourth ganglion. He (72) subsequently advocated the procedure for vascular disease of the lower extremities. In this approach the incision is made in the posterolateral lumbar region to extend from the twelfth rib above to the crest of the ilium below and then to curve anteriorly and inferiorly to a point just below the anterior superior spine of the ilium (Fig. 9, A). The oblique and transverse muscles of the abdomen as well as the lumbodorsal fascia are divided along the lateral border of the lumbar quadrate muscle. The posterior and posterolateral parietal peritoneum is then mobilized forward to expose the medial aspect of the iliopsoas muscle and the anterolateral border of the bodies of the lumbar vertebræ between which the lumbar sympathetic trunk lies. This approach is somewhat difficult in muscular and obese patients and has the added disadvantage of producing considerable operative trauma to muscle tissue. A much simpler procedure that affords even better exposure is the anterolateral extraperitoneal approach first described by Leriche (46, 49) in 1926. This approach has been subsequently modified by various surgeons. The procedure as described by Leriche and first performed by him in 1925 consists of making a slightly curved incision with its convexity outward along the anterolateral aspect of the abdomen from just below the costal margin above to a point about 3 centimeters medial and inferior to the anterior superior iliac spine (Fig. 9, C). The patient is placed on the table with the operative side elevated to an angle of approximately 30 degrees. The fibers of the external oblique muscle and aponeurosis are separated in the direction in which they run (Fig. 10). The internal oblique and transverse muscles of the abdomen are divided (Fig. 11). The authors have found this unnecessary if good muscular relaxation is obtained and for this reason employ spinal analgesia. Accordingly these muscle fibers are separated and not severed (Fig. 12). The transversalis fascia is thus exposed and incised, care being taken not to incise the parietal peritoneum (Fig. 12). By blunt dissection the posterolateral and posterior parietal peritoneum is mobilized medially to expose the iliopsoas muscle. Broad deep retractors are used to retract the peritoneum medially and under direct visualization the lumbar sympathetic trunk and ganglia are readily exposed lying between the medial border of the iliopsoas muscle and the anterolateral border of the bodies of the vertebræ covered by loose adventitious tissue (Fig. 13). It should be realized that the genitofemoral nerve that lies on the anterior aspect of the iliopsoas muscle may lie sufficiently medial to be confused with the lumbar sympathetic chain (Fig. 13). However, it may be readily distinguished from the latter by the fact that it has no ganglia or rami and never lies against the vertebral bodies. On the right side it is necessary to retract gently the vena cava as this structure usually overlies the trunk. Greater care must be exercised in freeing the chain on this side because the lumbar veins usually course anterior to it and accidental tearing of these veins produces annoying hemorrhage. Blunt hooks are used to pick up the chain and the rami are freed by careful blunt dissection with small firm gauze tampons applied to the end of long curved forceps. The second, third, and fourth lumbar ganglia and intervening trunk are excised (Fig. 13).

Slight modifications of this procedure have been described by a number of surgeons. Harris uses a transverse incision that extends from the lateral border of the quadrate lumbar muscle to the umbilicus (Fig. 9, E). A somewhat similar incision is employed by Flothow and the muscle fibers are split in the direction in which they run (Fig. 9, F). Pfeiffer and Livingston (65, 66) (Fig. 9, D) and more recently Pearl described more oblique anterolateral incisions (Fig. 9, H). Smithwick (76) employs an inverted L-shaped anterolateral incision (Fig. 9, J). Rees has described an anterior extraperitoneal approach for bilateral lumbar sympathectomy through a single incision. This consists of a Y-shaped incision with the tail of the Y extending longitudinally in the midline below the umbilicus and the two arms of the Y extending upward on each side of the umbilicus (Fig. 9, G). On both sides the anterior rectus sheaths are incised and the rectus muscles split. The posterior rectus sheath is similarly incised and the peritoneum and its contents are mobilized medially.

Because no preganglionic fibers join the sympathetic trunk below the fourth lumbar ganglion, Daniélopolu (15, 16) and others have considered too extensive the classical operation of resection of the second to the fourth ganglia, inclusive. The procedure which Daniélopolu, Aslan, and Marcan term "interlumbosacral sympathectomy" and which consists of section of the chain at the fourth ganglion is considered sufficient to interrupt vasoconstrictor impulses to the foot. On the other hand, Fontaine and his co-workers and Derom have shown convincingly by experimental investigations that in order to obtain a maximum vasodilatation in the lower extremity it is necessary to resect the first lumbar ganglia as well as the second, third, and fourth.

It is common knowledge that peripheral vasoconstriction can be initiated by reflex activity of the autonomic nervous system and also by an increased secretion of epinephrine. Such stimuli as exposure to cold and emotional excitement produce vascular spasm by reflex excitation of vasoconstrictor impulses to blood vessels and by reflexly increasing epinephrine secretion. Thus the mechanism of peripheral vasoconstriction under such circumstances may be humeral as well as neurogenic. Whereas the neurogenic constrictor activity may be diminished by sympathectomy, this procedure may have little influence on the humeral factor. Numerous observers have shown that the humeral factor in some instances may play a significant rôle in vasospastic functional and vasospastic organic conditions. On this basis and in an attempt to decrease also the reflex activity of this humeral factor Leriche, Pereira, and DeBakey (51) advocated simultaneous resection of the splanchnics and first and second lumbar sympathetic ganglia in vasospastic functional and vasospastic organic peripheral vascular disease. This may be readily performed with little or no technical difficulty through a new extraperitoneal approach which they (51) describe. The patient is placed in the lateral decubitus position with the back inclined slightly posteriorly and a pillow under the lumbar region (Fig. 14). A transverse incision about 10 to 12 centimeters in length is made just below the costal margin to extend from a point just anterior to the midaxillary line to the lateral border of the sacrospinal muscle (Fig. 14). The fibers of the external and internal oblique muscles are separated and incised to expose the fibers of the transverse muscle of the abdomen which are separated in the direction in which they run and the transversalis fascia which is incised to expose the peritoneum and retroperitoneal fascia (Fig. 14). This retroperitoneal fascia is gently mobilized forward and held in place by means of deep broad retractors thus exposing the anterior aspect of the lumbar quadrate muscle, the psoas muscles, and the diaphragmatic crura (Fig. 15). The greater and lesser splanchnics will be found to emerge from between the diaphragmatic crura and to pass somewhat medially and transversely to enter the semilunar ganglion. More medial and just below these structures will be found the first and second lumbar ganglia lying between the anterolateral aspect of the vertebral bodies and the iliopsoas muscle (Fig. 15).

## SUMMARY

1. The bases for rational therapy in peripheral vascular disease are discussed.

2. Peripheral vascular disease merely signifies a disturbance or actual diminution in the normal amount of circulating blood to a part and is usually the result of a varying diminution in the normal caliber of the peripheral vessels. This decrease in intraluminary volume may be caused by obliterative structural change, by abnormal spasticity, or by both, depending upon the type and the stage of the disease.

3. Effective therapy aims at improvement in circulation or increase in blood supply to the part which cannot be accomplished by an attack upon vessels that have already undergone structural change. Vasospasm, on the other hand, is a physiological or functional derangement which can be satisfactorily influenced by appropriate therapy.

4. Because vasospasm is the one controllable factor, the determination of its presence or absence and its extent are of decisive importance.

5. Therapeusis in peripheral vascular disease consists of measures aimed to improve the peripheral circulation and may be divided into two large groups: (1) conservative measures and (2) radical procedures.

6. Conservative measures are indicated in all cases of peripheral vascular disease except in acute vascular catastrophes and in the rapidly progressive peripheral vascular disturbances. The conservative measures consist largely of two groups: (1) those which are directed toward the elimination of all factors which increase vasospasm and (2) those factors which produce vasodilatation. Of the former, emotional disturbances, environment, and tobacco are the most important. Of the latter, application of heat and drugs, and the performance of vascular exercises are the most significant.

7. Whereas many of these conservative measures are justified and are usually sufficient to pro-

duce complete relief of symptoms, in the rapidly progressive case and especially in the case associated with a prominent degree of vasospasm, attack upon the sympathetic nervous system is considered desirable. The concept that in these vasospastic states sufficient vasoconstrictor impulses are transmitted over the sympathetic pathways to cause diminished circulation and that the release of these impulses may be enough to permit the return of circulation to normal forms the rational basis for sympathectomy. Interruption of impulses over sympathetic pathways may be accomplished by chemical block or by resection.

8. Chemical block of the regional sympathetic ganglia in peripheral vascular disease is considered a conservative procedure because of its efficacy, its simplicity and facility of performance, and its economic advantages.

9. In the presence of marked vasospasm in patients with impending vascular catastrophes or in those in whom conservative measures fail to relieve the vascular manifestations, radical therapy is justified. Sympathetic denervation of the affected part, however, should be performed only after the demonstration of vasodilatation following the diagnostic test of procaine hydrochloride block.

10. The factors which have been considered for the comparative failure of cervicothoracic sympathectomy to maintain chronic vasodilatation are reviewed and critically analyzed.

11. The technical considerations in the performance of cervicodorsal and lumbar sympathectomies for peripheral vascular disease are historically reviewed, described, and illustrated.

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# THE TREATMENT OF EXTENSIVE WOUNDS

## Notes on Six Cases in Which the Injuries Were Caused by a Circular Saw

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IN rural and agricultural districts, where small farms predominate, serious accidents are common and severe injuries of soft tissues and osseous structures in combination frequently result therefrom. Their treatment presents a real problem in reconstructive surgery in which the early restoration of normal structure and function are the ideal criteria of successful therapy. Unfortunately such perfect results are not always possible, but, in striving for those standards, certain essential principles of surgical treatment are imperative. These details fall chronologically into 3 groups: pre-operative, operative, and postoperative. Each group will be discussed separately, and the illustrative cases reported briefly thereafter.

1. *Pre-operative.* When the patient is first seen, bleeding of any consequence should be immediately arrested and all lesions in which there is a break in the continuity of the skin should be protected from further exposure to infection with sterile dressings. Before transportation all suspected and obvious fractures should be immobilized by temporary splints. After complete physical examination has revealed no evidence of intracranial or intra-abdominal injury, a liberal dose of morphine may be administered for relief of pain.

The arrest of hemorrhage, the immobilization of broken bones, and the control of pain are all highly important contributions toward the prevention of traumatic shock. If this condition be present when the patient is first seen, or develops subsequently in spite of these prophylactic measures, its immediate treatment must receive primary consideration before any surgical procedures are undertaken. During this period, frequent observations of the blood pressure, pulse rate, and respiratory rate should be made and recorded on a graphic sheet in order that the surgeon's clinical impression of the patient's condition may be supplemented by a visual record.

When these vital signs have become stabilized at a normal, or nearly normal, level all injured extremities should be examined carefully to determine the integrity of motor and sensory nerves, of muscles, and of tendons. This procedure is extremely important if the extremity is subsequently to be encased in a cast or even supported by splints.

2. *Operative.* Operative treatment begins with the choice of the proper anesthetic. Unfortunate and undesirable complications—cyanosis, vomiting, aspiration of particles of food, and asphyxia—occasionally follow the use of a general anesthetic soon after a meal. Local infiltration or blockage with novocain is preferred whenever satisfactory anesthesia can be obtained by this method. Local anesthesia also allows the patient, during the operation, to carry out active muscular contractions which afford valuable assistance in the identification of proximal ends of divided muscles and tendons. Spinal anesthesia is useful in injuries and fractures of the lower extremities but is definitely contra-indicated in patients who are on the verge of, or have just recovered from, shock. It is also undesirable in patients with hypertension.

Preparation of the operative field is an important part of every surgical procedure and becomes increasingly important in the treatment of mutilated wounds when the skin has been abraded and recently soiled with gross dirt, the subcutaneous tissues lacerated and devitalized, and the deep structures contaminated by foreign matter. The exposed area should be covered with one or more sterile sponges while the skin is cleansed with green soap, shaved from the edges of the wound toward the periphery, rewashed with soap, and scrubbed gently with some antiseptic solution. Alcohol and ether or a dilute solution of bichloride of mercury are effective and produce little necrosis of tissue. In draping, sterile towels should be placed close to the edges of the wound. Before complete exploration is carried out all devitalized and necrotic tissue should be excised, gross particles of dirt and other foreign bodies removed, and the wound irrigated from the depths outward with warm saline solution, or some very mild antiseptic. All viable tissue should be carefully preserved to be utilized later in the repair.

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The wound may then be thoroughly explored to determine the extent of injury to bones, muscles, tendons, and nerves. The use of a tourniquet is frequently of great assistance in obtaining a dry, bloodless field, and is imperative when major vessels have been divided. The ends of broken bones should be opposed and frequently stabilized by some form of internal fixation. Divided nerves and tendons must be accurately approximated, preferably with sutures of fine silk. The tourniquet should be removed and all bleeding points ligated with the same material before the wound is closed. It is unwise to use both silk and catgut in the same wound.

If the patient is seen within 6 hours from the time of the accident, tissues handled gently, and the aforementioned principles observed, drainage is seldom necessary; after 6 hours, it becomes more imperative as the interval of time increases. If tissues cannot be closed without tension, either some immediate plastic procedure or later secondary operation is necessary for the repair of tendons and nerves. Should the wound become infected, particularly with streptococcus, any secondary repair must be postponed for at least 8 to 12 months.

Some form of external fixation is essential for all injuries of bones, tendons, and nerves should be regarded as part of the operative procedure, and applied before the patient leaves the operating table. Extremities must be placed in such a position that divided tendons will be relaxed, and muscles, the nerve supply of which has been interrupted, will be at rest.

*3. Postoperative.* After operation immobilization should be maintained until healing is complete but may be interrupted daily for active and passive motion, within the limits of pain; this should be instituted as early as possible and supplemented by physical therapy. When motor nerves have been severed, muscular tone should be maintained by electric stimulation and massage until regeneration has occurred.

In order to appraise one's results accurately the patients must be followed until full recovery has taken place or the disability has become stabilized and permanent.

## REPORT OF CASES

In each of the following cases the injuries were caused by contact with a portable, circular buzz-saw. Trauma inflicted by such an agent produces extensive lacerated wounds of muscles, tendons, and nerves with communicating injuries of bones and joints which are more comparable to wounds of war than any others seen in civil practice.

CASE 1. Hospital No. 7102. C. B., a farmer, 26 years of age, slipped and fell onto a rotary saw in such a manner that the volar surface of the left wrist came in contact with the whirling blade. He sustained a deep, lacerated wound with widely separated edges, division of the radial and ulnar arteries, the median and ulnar nerves, and the tendons of the palmaris longus, the flexor carpi radialis, the flexors sublimis and profundus digitorum.

At operation the wound was cleansed and débrided, the arteries ligated, the nerves and tendons approximated with interrupted sutures of fine silk, and the wrist immobilized in slight flexion, with a volar splint of plaster. Physical therapy and passive motion within the limits of pain were instituted on the tenth day. Eleven months later all motions of the hand and fingers were normal save adduction of the thumb and little finger; there was some atrophy of the thenar and hypothenar eminences (Fig. 1). The patient was able to distinguish pain, light touch, and temperature in the palm down to the palmar-phalangeal creases. He was working with a pick and shovel and was able to perform all types of manual and agricultural labor without discomfort or disability. Four years later the condition was unchanged; he considered the function of his hand essentially normal.

CASE 2. Hospital No. 7265. R. C., a farmer's wife, 36 years of age, slipped while assisting with the operation of a rotary saw and fell forward onto the whirling blade. She received a deeply lacerated wound through the dorsal half of the left forearm below the elbow. The radius and ulna were divided and the elbow joint was widely opened, exposing the capitellum of the humerus and the jagged proximal end of the distal fragment of the radius; the radial head was absent (Fig. 2). The wound contained sawdust and fragments of cloth. No major vessels or nerves were severed.

Under nitrous oxide and oxygen anesthesia the skin was scrubbed with green soap and sterile water, shaved, and cleansed with alcohol and a solution of mercuric chloride. All gross débris was removed and the edges of the skin, the devitalized subcutaneous tissue, and muscle were excised. The cavity of the joint was irrigated with warm, normal saline solution. The fragments of the ulna were approximated to one another with two sutures of silver wire and the spicules of the shaft of the radius were removed with a rongeur. The end of the bone was placed in contact with the capitellum of the humerus (Fig. 2), and the capsule of the joint was closed with fine silk. The muscles, subcutaneous tissues, and skin were approximated without drainage by interrupted sutures of the same material and the wound was protected with silver foil. The forearm was immobilized in supination with the elbow at a right angle by anterior and posterior plaster splints.

Subsequently, some posterior angulation of the ulna occurred at the site of fracture and could be corrected only partially. Seven weeks after the accident union was firm both by clinical and fluoroscopic examinations. Active physiotherapy was continued and 5 weeks later the forearm could be flexed to a right angle and extended to within 20 degrees of normal; the hand could be rotated to mid-position from full supination. The patient was able to feed herself with the left hand, comb her hair, supinate the hand completely, and to pronate it by rotating the humerus. Flexion and extension of the wrist and fingers were normal. Four and one-half years later flexion at the elbow had improved only slightly, extension at the elbow and pronation of the hand were unchanged (Fig. 2). She was able to do all her own housework and some work about the farm and in the fields.

CASE 3. Hospital No. 7514. J. M., a boy, aged 16 years, was helping a neighbor cut wood with a rotary saw when he

Fig. 1. Case 1. Male, aged 26 years; lacerated wound of wrist; division of radial and ulnar arteries, median and ulnar nerves, tendons of flexor carpi radialis, palmaris longus, flexors sublimis and profundus digitorum. Photographs taken 11 months after injury.

lost his balance and fell forward until the dorsal surface of the left forearm came in contact with the whirling blade. Immediately after the accident he was unable to extend or abduct the fingers or to abduct the thumb; dorsiflexion of the wrist was limited. Exploration of the wound under anesthesia disclosed complete division of the extensor carpi ulnaris, extensor communis digitorum, extensor carpi radialis longus, and the abductor pollicis longus; the ulna was divided obliquely and the radius was partially severed (Fig. 3); no nerves or major vessels were injured.

The fragments of the ulna were approximated with one suture of silver wire reinforced with a double band of the same material around the shaft (Fig. 3). The muscles were sutured with silk and the subcutaneous tissues and skin were closed in layers without drainage. The arm was immobilized in midposition with 90 degrees' flexion at the elbow by molded splints of plaster. Passive motion and physical therapy were instituted at the end of 3 weeks. Seventeen months after the accident, flexion and extension of the elbow, wrist, and fingers, abduction and adduction of the thumb and fingers, were all normal (Fig. 4).

CASE 4. Hospital No. 9001. A. B., a farmer's daughter, aged 15 years, was helping her father operate a rotary saw when the whirling blade of the machine broke and a flying fragment therefrom struck her in the face and anterior thoracic wall.

She sustained a deep laceration of the right side of the forehead extending into the frontal sinus, superficial abrasions of the upper and lower eyelids, a ragged, lacerated wound of the right cheek extending into the maxillary antrum, division of the right nostril and the end of the nose which was attached only by a small cutaneous pedicle at the junction of the upper lip and septum, lacerations of the upper and lower lips and chin, and a deep, widely gaping

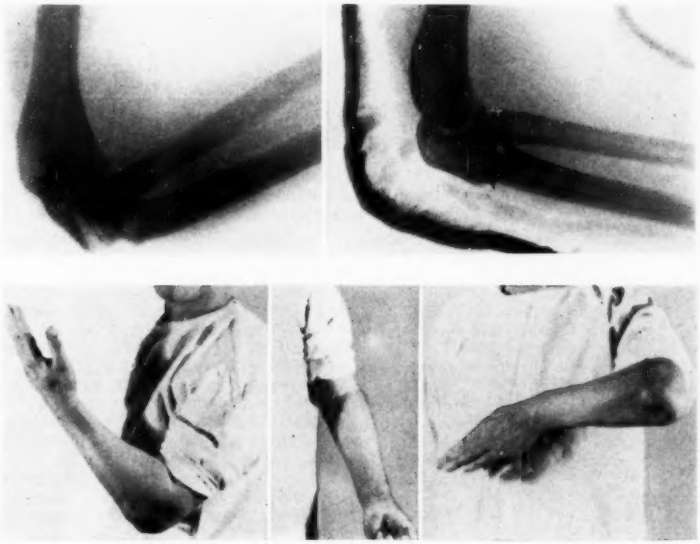

Fig. 2. Case 2. Female, aged 36 years; lacerated wound of elbow; compound fractures of radius and ulna; avulsion of radial head. Roentgenograms before and after reduction; photographs 6 years later showing flexion and extension at elbow.

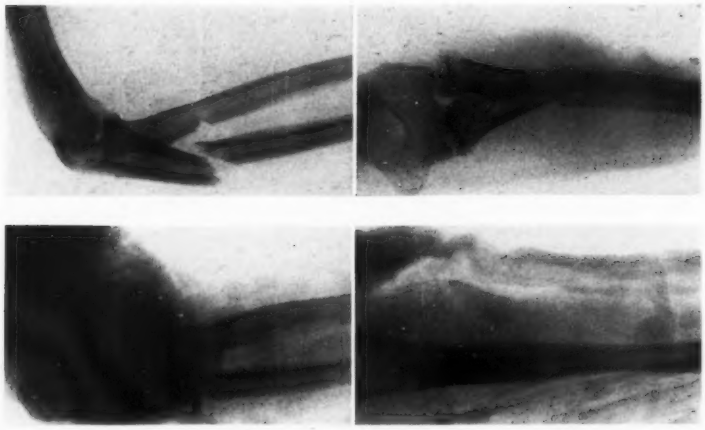

Fig. 3. Case 3. Male, aged 16 years; compound fracture of radius and ulna; division of extensor carp. ulnaris, extensor communis digitorum, extensor carpi radialis longus, and abductor pollicis longus. Above, Before reduction; below, after reduction and fixation with silver wire.

Fig. 4. Case 3. Seventeen months after injury. Flexion and extension at elbow; extension and abduction, flexion and adduction of fingers and thumb, and dorsiflexion at wrist, all normal.

wound of the anterior thoracic wall which extended through the clavicle and down to the upper six costal cartilages (Fig. 5).

Under local anesthesia the wounds were carefully débrided and closed in layers without drainage. The clavicle was immobilized with a metal cross. The sutures were removed from the face and nose on the second and third days; some superficial sloughing occurred about the right nostril farthest from the pedicle (Fig. 5).

Two months after the accident a small, wedge-shaped defect was present in the ala of the right nostril and the other scars of the face were still red and prominent (Fig. 5). Five years later the wounds of the face were scarcely noticeable even at close range but a small defect was still present in the nose and the scars of the thoracic wall were prominent.

Case 5. Hospital No. 9066. J. S., a farmer, 37 years old, while operating a buzz saw, was struck on the left shoulder by a large, jagged, irregular fragment of a bursting flywheel, traveling at high speed. He was rendered temporarily unconscious and was in a profound degree of shock from loss of blood when he reached the hospital 2 hours later. Examination showed a wide, gaping, lacerated wound of the anterior aspect of the left shoulder and upper portion of the thoracic wall from which venous and arterial blood was oozing (Fig. 6). All motions of the shoulder and left forearm were extremely painful.

One thousand cubic centimeters of a warm 5 per cent solution of glucose was given intravenously and the patient was grouped and cross-matched with a suitable donor for transfusion. A portable roentgenogram disclosed comminuted fractures of the anatomical and surgical necks of the humerus, compound fractures of the acromion and coracoid processes of the scapula with a loose fragment overlying the glenoid fossa, a linear fracture in the wing of the scapula below the glenoid, separation of the acromioclavicular joint (Fig. 6), and a simple fracture of the shaft of the radius.

Following transfusion with 500 cubic centimeters of whole blood, the patient's condition improved and he was moved to the operating room. The skin around the wound was shaved, scrubbed with green soap, sterile water, alco-

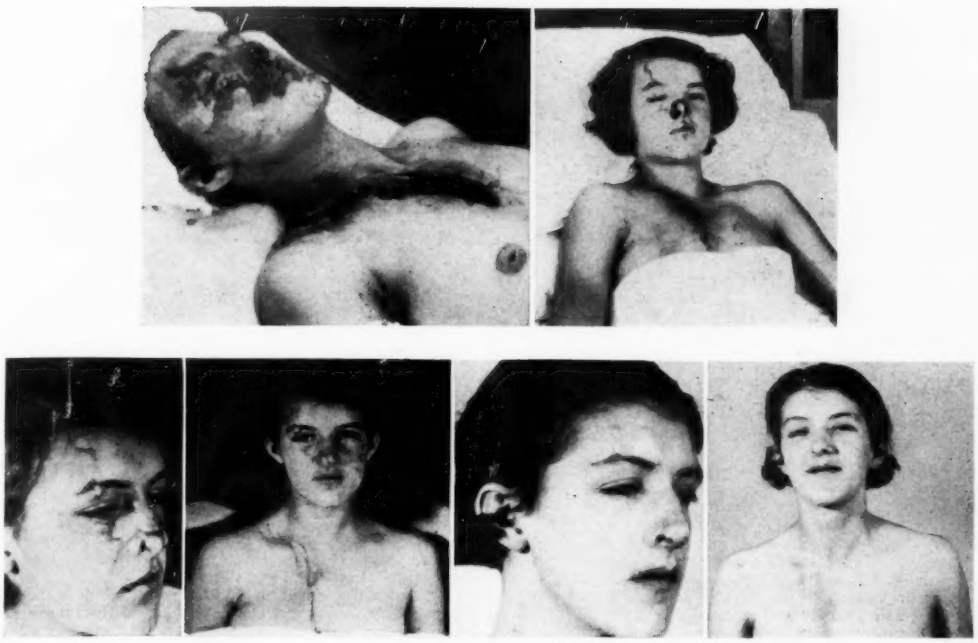

Fig. 5. Case 4. Female, aged 15 years; compound fractures of frontal bone extending into sinus, of superior maxilla extending into maxillary sinus, and of clavicle; lacerated wounds of forehead, eyelids, cheek, nose, lips, chin, and thoracic wall. Above, Photographs on admission to hospital, and 3 days later; below, left, face and chest 2 months after injury and face and chest 3 and 5 years later.

hol, and a weak solution of bichloride of mercury. The wound was gently irrigated with bichloride and the edges were infiltrated with novocain. All the devitalized tissues from the sternum to the mid-axillary line were cut away and numerous particles of grit and dirt were removed. The coracoid process was sutured to the scapula with silver wire. Five Dakin tubes were inserted, the edges of the skin were excised, and a sterile dressing was applied. The arm was immobilized in abduction at a right angle with a Jones humerus traction splint.

The following day the patient had an abrupt elevation in temperature to 105 degrees F. and the pulse rate to 136. Examination showed diffuse fullness and tenderness of the thoracic wall below the axilla. A moderate amount of serosanguineous, watery fluid welled up into the wound when pressure was applied over this area and short-chained gram positive streptococci were seen in smears made from this material. Counter drainage was established and 10,000 units of antistreptococcus serum prepared by the New York State Laboratory, was administered intramuscularly. The following day his clinical condition was somewhat improved and another 10,000 units was given. The temperature and pulse rate gradually fell to normal on the tenth day when dakinization was discontinued. The large defect slowly filled in with granulation tissue and was later covered with pinch grafts. At the end of 7 weeks, traction was discontinued and physical therapy was instituted. Clinically and fluoroscopically, the fragments of the humerus were in good position (Fig. 6). He was discharged 59 days from the date of the accident.

Physical therapy was continued for 6 weeks. Two and one-half months later the patient was unable to abduct the arm voluntarily beyond an angle of 30 degrees from the plane of the body; passive motion was entirely free and painless in all directions; pronation and supination of the hand were normal. Sensory examination revealed an area of anesthesia on the anterior, lateral, and posterior surfaces of the arm corresponding with the distribution of the sensory fibers of the axillary nerve, which also furnishes the entire motor supply to the deltoid muscle. It was then obvious that the limitation of active abduction was caused by undetected damage to the axillary nerve at the time of the accident.

Five years after the injury the bones were in satisfactory position (Fig. 6). A small defect was apparent in the soft tissues of the anterior aspect of the shoulder; the skin was partially adherent to the ribs and intercostal muscles. In the supine position the patient was able to abduct the arm normally but when erect could not elevate it beyond an angle of 30 degrees from the vertical plane (Fig. 6). In spite of this disability he was able to do all the work on his farm which included pitching hay for 20 cows.

CASE 6. Hospital No. 11671. A. M., a farmer, aged 37 years, sustained a traumatic amputation of the right hand while operating a rotary saw. He was unable to recall how the accident occurred but from the nature of the injury it is probable that he fell forward onto the whirling blade. Examination disclosed complete division of all the skeletal structures of the wrist from the ulnar side of the carpus transversely across to the radial side. The hand was at-

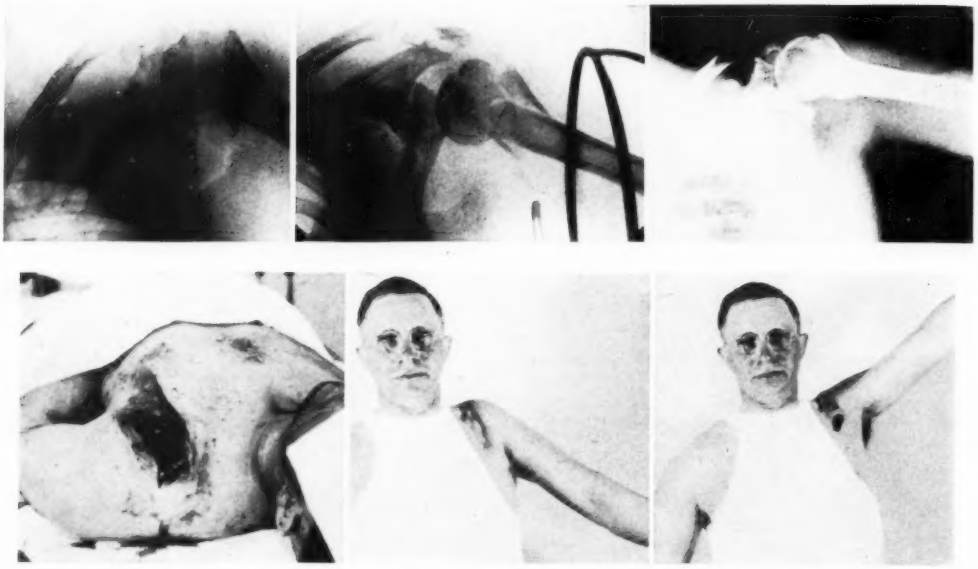

Fig. 6. Case 5. Male, aged 37 years; compound comminuted fractures of surgical and anatomical necks of humerus, of wing and coracoid and acromion processes of scapula; dislocation at acromioclavicular joint; simple fracture of radius; lacerated wound of thoracic wall and shoulder. Above, on admission, after fixation, and 5 years later. Below, on admission and 5 months later.

tached only by 2 badly traumatized tendons and an isthmus of skin at the base of the thumb.

Under general anesthesia the wound and surrounding area were thoroughly cleansed, a flap of skin and subcutaneous tissue was reflected from the dorsal surface of the thumb, and the amputation of the hand was completed by dividing the 2 remaining tendons. The radial and ulnar arteries were ligated and the tourniquet was loosened. Several of the carpal bones were removed and all devitalized tissue was excised. The prepared flap was utilized to cover the radial side of the stump, and the ulnar side was partially closed by undercutting and approximating the skin on the dorsal and volar surfaces of the wrist. Gutta percha, sterile gauze, and a splint were applied.

The immediate convalescence was complicated by an indolent infection of the wound due to Staphylococcus aureus. Drainage persisted from several small sinuses for 3 months after which the stump healed and contracted satisfactorily. The skin and subcutaneous tissues were freely movable on the deeper structures and some motion was present at the radiocarpal joint. The patient learned to write with his left hand and has otherwise adjusted himself so well to the deformity that he can do all the varied jobs in the routine life of a farmer and does not desire an artificial hand.

## SUMMARY

In the care of extensive wounds involving muscles, tendons, nerves, bones, and joints, careful pre-operative observation and treatment, meticulous operative technique, and prolonged postoperative supervision are essential in order to secure good functional and anatomical results.

Six cases illustrating wounds of this type due to contact with a circular saw, have been reported in some detail.

# PRESERVED AND FRESH HOMOTRANSPLANTS OF CARTILAGE

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IN 1928, following reports of the use of boiled bone flaps in neurosurgery, it was thought that cartilage might be preserved or refrigerated so that it could be used at a later date as a subcutaneous prosthesis. A summary of observations made over an 11 year period and illustrations of clinical results are presented here.

*Source of preserved homotransplants of cartilage.* A constant supply of foreign cartilage is somewhat difficult to maintain. It has been obtained from other patients having autogenous transplants done, and from other operations on the thorax. Autopsies give the easiest and most abundant source; the subject, of course, should be of known age and race, and should not have had any contagious disease. The cartilage should preferably be from a young adult and free of calcification. Cadaver material certainly is not very esthetic, although ear cartilage has been used, somewhat enthusiastically by Kirkham.

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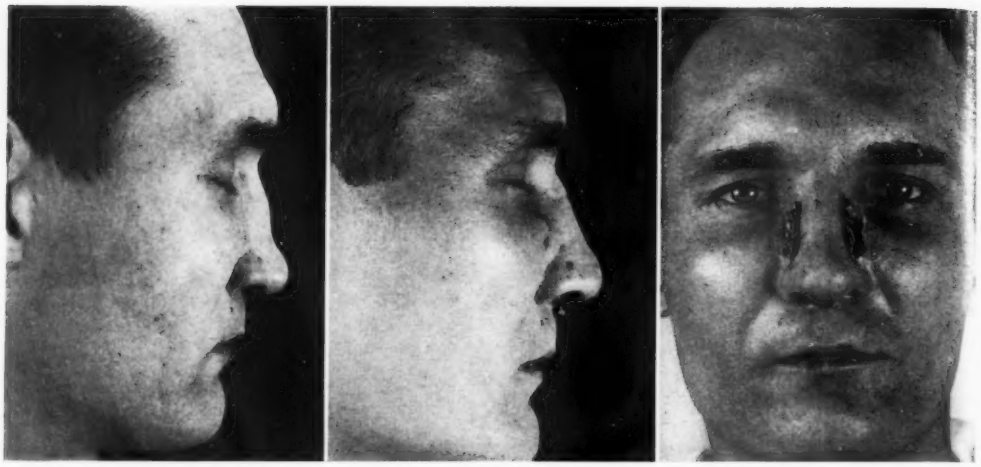
*Storage or preservative.* Alcohol was originally employed as a preservative for simplicity and safety, the cartilage being thoroughly washed in saline before implantation. This method eliminates the necessity of sterile precaution in handling before storing. Other preservatives, refrigeration and freezing may also be used, and freezing might be preferred if a good source of sterile cartilage could be had.

It is preferable to store the cartilage quite clean but it is difficult to strip the perichondrium without damaging the cartilage and, for this reason, it may be best to store it partly clean and then cut the pattern out cleanly at the time of operation.

*Zoografts.* In the early work, suitable cartilage from other animals was sought, but sheep, cats, and puppies all have bone through the center, and beef cartilage causes too much reaction in the tissues to be retained. The tip of the shoulder blade in beef does offer a very easy source of huge pieces, however, and, if a method of avoiding the

Fig. 1. a, left. Deformity following autogenous cartilage transplant (done elsewhere) with calcification and distortion of the cartilage, rendering it useless. b, Result of preserved cartilage transplant. Complete mobilization of the lateral bony walls, was necessary for narrowing after the distorted cartilage was removed; through and through wires were put in as in Figure 2c; as it is often best not to combine an extension osteoplastic with a fresh cartilage transplant a preserved cartilage was used as a temporary subcutaneous prosthesis. It was healed promptly, however, and is in good condition more than 2 years later.



a b c

Fig. 2. a, Depression of cartilaginous dorsum with elevation and disappearance of the columella. b, Complete dorsal, columellar and nasal spine prominence restored in a single operation, by mobilization of the bones and implanting an L-shaped preserved cartilage as shown in Figure 3. c, Through-and-through silver wires fastened over lead plates to maintain narrowness after mobilization of the lateral bony walls.

marked reaction to it can be developed, the problem of subcutaneous prosthesis will be greatly helped.

*Other materials used for implantation.* Ivory seems to be satisfactory in many instances and its preparation can be done accurately to pattern, but many of these transplants have given trouble and have been extruded after years. In animals, wood, rubber and celluloid have been retained but have not been satisfactory clinically. Some of the newer plastics and metals such as vitallium may be successful, but a few years' observation will be necessary.

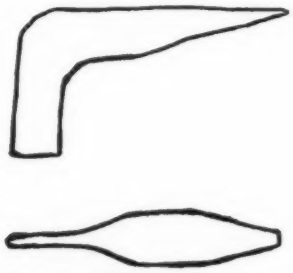


Fig. 3. Diagram of L-shaped nasal cartilage transplant. a, above. Side view of single piece of cartilage to restore nasal contour with support at the nasal spine and above. This type can be put in luetic noses with only a small amount of tissue left in the columella. If the whole cartilage is lost but the mucosa remains, even a larger sheet may be used practically to replace the septum. The upper end is always placed under the periosteum if possible, and this applies to all regions; if only a small pocket of periosteum can be prepared, the best possible support is then obtained. The large piece is best obtained by cutting it out of an angle or where two cartilages are united. b, Top view showing breadth above and thinning below to avoid widening of the tip and columella. If necessary to gain lateral bulk, wide side wings may be left on or extra pieces put in. Both views are diagrammatic. The general shape is cut out and then trimmed down to pattern.

The best possible prosthesis would be one that could be safely injected and molded and would then retain its shape, and because of this ultimate desirability, an injectable suspension of cartilage has been considered, especially for small defects. Paraffin is still thought to be dangerous enough to avoid.

*Gross and microscopic appearance of fresh and preserved cartilage.* Human costal cartilage appears to be somewhat unique in that its exact counterpart in other easily available animals has not been found. It occurs in two main varieties—white and yellow—and may be calcified in spots or streaks, even in children. Calcification is almost sure to be present in older patients. The white and yellow appearances were formerly thought to be due to a larger number of cells in the white but, after the study of many sections, it is thought that the difference is probably in the hyaline material itself. Preserving the cartilage does not change its microscopic appearance except that the normal cell nucleus is lost and the pathological diagnosis might be made of necrosis because

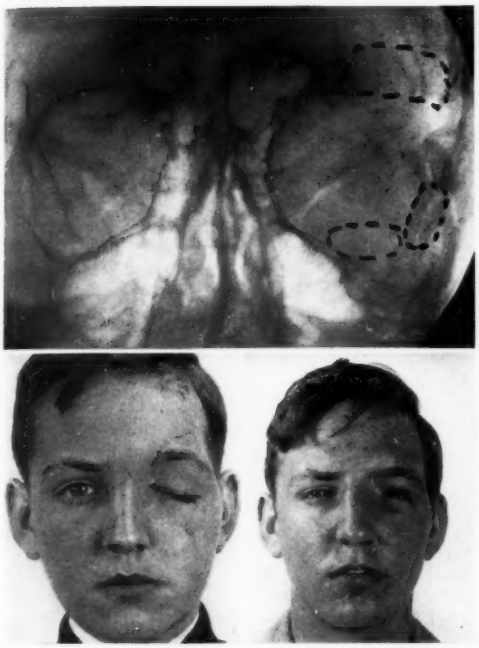


Fig. 4. a, above. Extreme crushing and loss of bone around the orbital borders, with areas of fresh homografts of cartilage, blocked in, to raise the globe, hold it medially and to form an upper orbital border. b, below left. Completely ptosed lid over the badly displaced globe. c, Result after the three pieces of fresh costal cartilage from the mother were put in place under local anesthesia, and the lid was elevated with fascial transplants. Shown after 1 year.

of this. When preserved in alcohol, the yellow type becomes more yellow, clearer, and harder—sometimes so hard as to be brittle and unsatisfactory for use. Curling takes place also but this is thought possibly to be one advantage, that is, to have the curling take place before it is used as a transplant. The white cartilage usually stays white and maintains about its original consistency.

*Fate of preserved cartilage transplants in the tissues. There is undoubtedly reaction around these transplants that, in many instances,* will result in complete solution of the graft. They do not stand any infection well, as a rule, but have healed in satisfactorily following drainage from the wound in several instances. The experimental implantation of pieces in animals or in the abdominal wall of patients is not comparable to the clinical use because these beds are, undoubtedly, better than those about the nose and face where the material is usually needed. Because of the uniform good

Fig. 5. a, left. Complete loss of septal cartilage from infection. Following an early complete loss, the face doesn't elongate normally in this region and, therefore, it is thought imperative to try to restore the septum if possible. Patient seen before marked collapse had occurred. b, Result of a single L-shaped piece replacement of the septum with fresh cartilage from the father. An extra piece is stored in the epigastrium for possible future use.

results, at least of retention of the transplants in soft abdominal wall pockets, it is apparent that the best possible bed should be obtained in the face, and that the wound edges should be closed as thickly as possible.

If an especially poor bed is known to be present to receive the transplant it may be of some advantage to store it temporarily in the abdominal wall and use it after it has become firm in its new surroundings.

Repeated transplants of the same piece of cartilage have been successfully done, and it is thought that many may remain in the tissues permanently. However, as stated, it is definite that absorption takes place to some extent in all instances and complete loss may occur by a gradual process, without visible reaction, over a period of several months. This process is not always uniform and the transplant may appear actually scalloped.

*Clinical evaluation.* The benefits of preserved over fresh autogenous cartilage may be as follows: (1) no operation on chest of patient; (2) a large amount is available; (3) patterns can be made more easily; (4) probably not as apt to curve and distort tissue; (5) may be used as a temporary prosthesis either intentionally or as a necessity. The objectionable features are: (1) it is not very esthetic, especially if race or color is off, or if there has been some disease in the donor patient; (2) it is not as resistant to infection; (3) *it may be completely absorbed without infection;* (4) it needs an

especially good bed without tension on the wound; (5) if it becomes too hard, irregularities cannot easily be trimmed subcutaneously; (6) if one fails, it is probably best to repeat with fresh cartilage.

The patients in Figures 1 and 2 have had preserved cartilage transplants in the nose in place for as long as 3 years. Other areas in which it has been used are the cheeks, chin, jaw, orbit, forehead defects, and in the temporomandibular joint.

At this time the method is not offered as a replacement for fresh homogenous transplants but rather as a second choice substitution when, for some reason, the fresh homograft is not advisable. If the cartilage proves to remain only temporarily, a fresh transplant may be put in if necessary.

*Single-piece, L-shaped nasal cartilage transplants* are used routinely by cutting the pattern out of the angle of the cartilage. This avoids bending the cartilage, using two pieces, or risking the use of a single piece unsupported at the tip. It is put in through an incision down the columella (Fig. 3).

*Fresh cartilage transplants from other persons.* In children who do not have large enough costal cartilages to supply good pieces and in any adult who does not want his chest opened—when a fresh cartilage transplant is desired, it is thought that a fresh homotransplant may be used with practical certainty of success. The success of cartilage and fascia as free homografts is in contradistinction to skin which is known not to survive permanently (Figs. 4 and 5).

In using homotransplants of cartilage, it would be desirable to use a parent or near relative but this is probably not necessary.

*Metal pins through cartilage transplants to prevent distortion.* Any kind of cartilage transplant is apt to curl and cause deformity, and observations are being made on the use of a central pin of vitallium to try to maintain alinement of the cartilage.

# CARCINOMA OF THE BODY OF THE UTERUS

## Experience of the Mayo Clinic for Twenty-Four Years

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THE clinical characteristics of patients presenting carcinoma of the uterine body have been fairly well established. The great majority of patients fall in the postmenopausal group, as pointed out by Norris and Dunne, 69.5 per cent; Scheffey and Thudium, 52 of 68 patients; and Stacy, 63.3 per cent.

Maternity and trauma of childbearing have little or no influence on carcinoma of the fundus, for Norris and Dunne and others have found a high incidence of nulliparity in patients with this malignant lesion.

Leiomyomas occur very frequently in uteri subject to carcinomatous change. Taylor and Millen found an incidence of 40 per cent of leiomyomas in combination with carcinoma of the fundus, whereas other workers have found them slightly less frequent—Stacy, 37 per cent; Falls, 35 per cent; Norris and Dunne, 34 per cent. Falls found carcinoma occurring in 9.5 per cent of patients operated upon for leiomyomas. We have found no statistical studies concerning the factor of heredity in the genesis of cancer of the fundus.

The possibility that endocrine dysfunction may have some bearing on the genesis of fundal cancer has been suggested by recent studies. The term, endometrial hyperplasia, has been loosely used in the past to designate a non-atrophic endometrium in the postmenopausal uterus. Taylor and Millen found "endometrial hyperplasia" in 15 out of 34 cases of carcinoma of the corpus uteri in which specimens of non-cancerous endometrium were available for study. Of 99 control non-malignant cases in the same age group a non-atrophic endometrium was found in only 11 cases. In 6 of these cases the patients were less than 50 years of age; it occurred in only 5 of them after the age of 50 and in not a single uterus from a woman past 60 years of age. Payne found the incidence of carcinoma in association with postmenopausal hyperplasia to be 10.5 per cent. Novak and Yui found a similar high incidence of "endometrial hyperplasia" in association with cancer of the fundus.

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Herrell, in omitting the older "endometrial hyperplasia" from his terminology, and in classifying types of endometrium on the basis of physiological and pathological variations in the menstrual cycle and concomitant hormone changes, has done much to clarify our conception of the endometrium. In 50 cases of carcinoma of the fundus, he found a differentiative endometrium in only 2 cases. Both of these were from women in the premenopausal group. In the 48 remaining cases he found a proliferative type of endometrium, evidence of estrin effect. In 10 patients with fundal cancer he studied the estrin level in the urine and in 8 of these he found 5 or more rat units in a 24 hour sample. These observations suggest that endocrine imbalance may be in some way related to the genesis of fundal cancer, but, until more studies on the incidence of persistent estrin effect postmenopausally have been made, no definite conclusions may be drawn.

The late age of menopause in these cases found by Crossen (3) further suggests a persistent ovarian function as bearing on the causation of fundal cancer.

The characteristic symptoms of fundal cancer have been fairly well established. The most significant symptom is metrorrhagia, which has been reported as occurring in from 80 to 95 per cent of cases. Menorrhagia in patients before the menopause, while more often associated with benign lesions or endocrine disturbance, may occur as the only symptom of a malignant lesion. About one-third of Stacy's patients in the premenopausal group had menorrhagia, and half of the patients in Scheffey and Thudium's series who had not reached the menopause had profuse periods. An abnormal discharge has been found in different series of reported cases in an incidence of 30 to 60 per cent. Pain of the menstrual type has been found in 30 to 40 per cent of patients, but has not indicated necessarily an unfavorable prognosis.

That the lesion is usually of slow development is evidenced by the long duration of symptoms usually reported. Scheffey and Thudium found an average duration of symptoms of 9.5 months

in patients in the premenopausal group and 15.2 months in the postmenopausal group. Norris and Dunne's patients had symptoms on the average for 17.9 months before seeking medical attention.

The standard treatment for carcinoma of the uterine body is total abdominal hysterectomy with bilateral salpingo-oophorectomy. Vaginal hysterectomy has been used for patients for whom the risk is poor and who have small tumors, especially when associated with some prolapse. Irradiation has been, in most series reported, reserved for patients with inoperable lesions or for patients for whom the risk of operation was judged prohibitive.

Any comparison of the results of radiation and operation either alone or in combination must take into account the grade and extent of the lesion and the age and general condition of the patient to give an accurate basis for any conclusion. Most workers in reporting 5 year survivals count all untraced patients as dead. When anywhere from 10 to 30 per cent of patients are untraced the 5 year survival on this basis of calculation is bound to be poor. Thus in Norris and Dunne's series of 211 patients, 94 were alive 5 years, and 40 were not traced. This gives a survival of only 44.5 per cent of all cases, but 54.9 per cent of traced cases.

Morton, in reviewing the literature on carcinoma of the fundus for 1936, found 5 year cures ranging all the way from 29.4 to 60 per cent. In those cases in which operation was performed the 5 year salvage ranged all the way from 57 to 79.4 per cent. Interesting is the fact that the highest percentage of cure was reported in the cases in which operation was performed by Heyman who employs largely radiological treatment.

Scheffey and Thudium reported a 32.6 per cent relative 5 year cure employing both operation and irradiation; Ward and Sackett a 45.5 per cent 5 year survival with a 61.9 per cent survival for the surgically treated patients and a 35.6 per cent survival for those treated by irradiation alone. Stacy's 63.88 per cent 5 year arrests reported in 1929 compare favorably with the 63 per cent survival of the traced patients of Norris and Dunne on whom operation had been performed. Plate found 38 of 67 patients alive after 5 years.

Heyman has probably had as much experience with irradiation as anyone and he expressed the opinion that irradiation is only an adjunct to hysterectomy in cases in which the risk is good but offers much in the way of possible cure to the patient for whom the risk is poor and offers palliation in the inoperable case. Phaneuf, as well as Heyman, has pointed out the difficulties of securing adequate irradiation to all parts of a fundal cancer. Heyman has devised a method for spreading the radiation from radium to all parts of the uterine cavity, and results of a preliminary small series are favorable. Healey has found in uteri removed 4 to 10 weeks after irradiation evidence of persistent cancer in possibly 1 of 3 cases. "Often this is said to show marked irradiation change and to be non-viable." Bowing and Fricke have indicated the usefulness of irradiation, not as a substitute but as an adjunct to operation. Until at least comparable stages of growth are used for comparison no conclusions can be drawn from the results by any method of treatment.

Classifications of fundal cancer have been advocated by Crossen (3), Schmitz and Schmitz, and Heyman. Crossen's classification embraces 6 separate groups, all based on operative and pathological observations. The Schmitz' classification is entirely clinical, and they expressed the opinion that such a clinical classification is the only type one can use to compare results by separate methods of treatment. Heyman's classification is very simple, dividing patients into clinically operable, technically operable, clinically inoperable, and technically inoperable. It seems that for patients on whom operation has been performed some useful purpose can be gained by classifying the cases into somewhat smaller subgroups than Heyman does. His classification or one similar to it must certainly be essentially the one to use if one is to compare results by radiation and surgical operation.

We are presenting the results of an analysis of the cases of carcinoma of the uterine corpus seen at the Mayo Clinic from January 1, 1910, to December 31, 1933, inclusive. The clinical features, symptoms, pathological characters, treatment and 5 and 10 year results of therapy on all cases primarily treated at the clinic are presented in some detail. The results on recurrent cases are briefly summarized. For the sake of comparison the incidence and 5 year survival of patients with sarcoma of the uterus are given.

## MATERIAL

There was a total of 907 cases of fundal cancer seen in this period, of which 732 were cases of pure fundal carcinoma unassociated with other primary malignant lesion. In 22 there was carcinoma of both body and cervix so that the site of origin is doubtful. In 19 there was a complicating primary ovarian malignant lesion. There were 47 cases of recurrent carcinoma apparently arising

in the fundus and previously treated elsewhere. In 84 cases there was sarcoma of the uterus and in 3 cases sarcoma and carcinoma occurred in the same uterus. The total number of patients with carcinoma was 823 of whom 802 were traced 5 years or more; 799 of these were treated. Eighty-two of the 84 patients with sarcoma were traced a minimum of 5 years.

### CLINICAL FEATURES OF CARCINOMA OF THE BODY OF THE UTERUS

*Age.* The average age of the 732 patients suffering from pure carcinoma of the body of the uterus primarily treated here was 56.01 years. Figure 1 shows graphically the age distribution by decades. The highest incidence occurred in the sixth decade with 357 cases, or 48.7 per cent. The seventh decade followed next with 180 cases, or 24.6 per cent, surpassing the fifth decade with 134 cases, or 18.3 per cent. Thirty-nine were in the eighth decade, 2 were over 80 years of age, and 1 patient was 29 years of age. Only 20 patients were less than 40 years of age.

*Marital state and number of children.* In 730 cases the marital state and number of children were recorded. Table I shows these data.

*Menopause.* Two hundred and twenty-one patients had not passed through the menopause, whereas 510 had ceased menstruating prior to the onset of symptoms. For 1 patient this information was not recorded. The average age of the premenopausal group was 48.98 years. Those who had ceased menstruating gave an average age of 59.29 years. The average age at menopause of this postmenopausal group was 50.27 years, excluding 12 patients whose menstrual function had been abolished by surgical operation or radiation. In Table II we have shown the age distribution at menopause in these 498 patients and in a control group of 190 patients picked at random from the files of the Mayo Clinic during the same period. This latter group was selected only in that they were all 60 years of age or older and that they had not ceased to menstruate because of artificial means. The average age at menopause of the control group was 49.9 years. Statistically there is no essential difference in the average age or in the age distribution for the two series.

### SYMPTOMATOLOGY OF CARCINOMA OF THE BODY OF THE UTERUS

1. Menorrhagia was noted in 119, or 53.8 per cent, of 221 premenopausal cases. Its average duration was more than 4 years (49.6 months).

2. The most significant symptom was metrorrhagia. Six hundred and sixty patients, or 90.2 per cent, complained of bleeding at an abnormal time for a variable period, from 1 day to 17 years. The average duration of this symptom was 18 months.

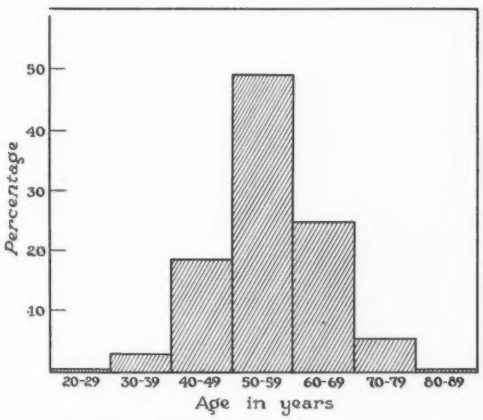


Fig. 1. Percentage distribution by age of carcinoma of the uterine body.

3. The next most important symptom was an abnormal discharge. This usually presented either as a yellowish mucoid discharge preceding onset of bleeding, or a thin watery leucorrhea following some months after the onset of the appearance of blood. Five hundred and two patients, or 68.6 per cent, complained of one or the other of these 2 types of leucorrhea which had persisted on an average for 16.4 months.

4. Pain was complained of by 204 patients, or 27.9 per cent. It had been present on an average of 13.2 months. The character of the pain was variable; many patients had a crampy pain of menstrual type, while others complained of an aching in the lower part of the abdomen or of the back, and some complained of a general lower abdominal soreness.

TABLE I.—FREQUENCY BY MARITAL STATE AND NUMBER OF CHILDREN OF WOMEN SUFFERING FROM CARCINOMA OF THE BODY OF THE UTERUS

| Single | Married—Number of children per woman | | | | | | | | | | | | | Totals |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | |
| 73 | 194 | 118 | 125 | 72 | 58 | 28 | 18 | 16 | 8 | 5 | 6 | 3 | 2 | 4 | 730 |
| Total number of children | 0 | 118 | 250 | 216 | 232 | 140 | 108 | 112 | 64 | 45 | 60 | 33 | 24 | 52 | 1,454 |

Number of children per woman: 1.99.
Number of children per married woman: 2.21.

TABLE II.—AGE AT MENOPAUSE OF PATIENTS WITH CARCINOMA OF THE FUNDUS AND OF A CONTROL GROUP

| Age at menopause, years | | Total | 25–29 | 30–34 | 35–39 | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | Average age |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Carcinoma of fundus | No. | 498 | 1 | 2 | 9 | 33 | 153 | 253 | 43 | 4 | 50.27 years |
| | Per cent | 100.0 | 0.2 | 0.4 | 1.8 | 6.6 | 30.7 | 50.9 | 8.6 | 0.8 | |
| Control | No. | 190 | | 3 | 2 | 15 | 61 | 94 | 12 | 3 | 49.9 years |
| | Per cent | 100.0 | | 1.7 | 1.1 | 7.8 | 32.1 | 49.5 | 6.1 | 1.7 | |

5. Loss of weight was not a feature, significant loss of 4 pounds or more occurring in only 199 cases, or 27.2 per cent of cases. The average weight loss of this group was 17.6 pounds.

6. Anemia. In 539 cases the concentration of hemoglobin in the blood was determined and of these, 340 cases gave normal values, and 199 were anemic. (Prior to 1929 the Dare hemoglobinometer was used as standard and 70 per cent or less was considered as indicative of anemia. Since 1929 the Cenco-Sheard-Sanford photelometer has been used. Since that time any hemoglobin level less than 12 grams per 100 cubic centimeters has been considered as indicative of anemia.)

### PATHOLOGY OF CARCINOMA OF THE BODY OF THE UTERUS

*Grade and extent of lesions.* There were 257 cases in which the patient was primarily treated here and in which the histological grade was determined according to the method of Broders on a basis of 1 to 4. Of these, 57 cases were classified in grade 1, 134 cases were in grade 2, 31 cases were in grade 3, and 35 cases were in grade 4.

In 467 cases it was possible to classify the growths as to extent of lesion. In 265 cases this was not possible. In the unclassified group we have included all cases in which the patient was treated by radiation and in which clinically a stage 4 growth had not been reached, as well as cases in which operation had been performed. Our system of grouping according to stage corresponds fairly closely to that of Schmitz and Schmitz except that in stages 1, 2, and 3 we have included only cases in which operation had been performed, whereas their classification is entirely a clinical one.

In stage 1 we have included only those cases in which the growth was limited to the endometrium. In stage 2, we have included all those cases in which the muscle was invaded, but in which the peritoneal coat had not been reached. Included in this group are several cases in which the growth had extended into the upper portion of the cervix but in which the origin was clearly in the fundus. We have placed all cases in which both fundus and cervix were involved and in which there was a question as to origin in a separate group, carcinoma of fundus and cervix. In stage 3 we have placed those cases in which the carcinoma had extended to the peritoneum with or without attachment to adjacent structures, as long as other structures were not grossly invaded by malignant tissue. In stage 4 we have placed all cases in which any structure outside the uterus itself was involved. This includes parametrium, tubes, ovaries, bladder, bowel, other contiguous structures, lymph nodes, and distant metastases. In some cases in which both ovary and fundus were involved in the malignant process it was impossible to tell which was the primary site or whether we were dealing with two primary tumors. If the lesion was apparently primary in the uterus with secondary ovarian involvement the case was classified in stage 4, unless the cell characteristics of the two tumors were sufficiently

TABLE III.—PERCENTAGE AGE DISTRIBUTION BY EXTENT OF LESION

| Stage | Age in years | | | | |
|---|---|---|---|---|---|
| | 30–39 | 40–49 | 50–59 | 60–69 | 70–79 |
| 1 | 8.9 | 28.2 | 40.2 | 20.3 | 2.4 |
| 2 | 0.8 | 17.9 | 52.8 | 25.3 | 3.2 |
| 3 | 2.6 | 16.9 | 57.1 | 18.2 | 5.2 |
| 4 | 1.3 | 22.9 | 49.4 | 26.4 | 0.0 |

TABLE IV.—PERCENTAGE DISTRIBUTION OF DURATION OF METRORRHAGIA BY EXTENT OF LESION

| Stage | No metrorrhagia | Duration of metrorrhagia | | | | |
|---|---|---|---|---|---|---|
| | | 0–6 months | 7–12 months | 13–24 months | 25–36 months | 36 months plus |
| 1 | 18.0 | 46.1 | 11.2 | 11.3 | 5.6 | 7.8 |
| 2 | 8.8 | 38.2 | 13.7 | 22.4 | 7.6 | 9.3 |
| 3 | 5.2 | 28.5 | 20.8 | 28.6 | 5.2 | 11.7 |
| 4 | 12.3 | 24.6 | 24.6 | 15.6 | 7.3 | 15.6 |

TABLE V.—SYMPTOMS OF CARCINOMA OF FUNDUS ACCORDING TO GRADE OF MALIGNANCY*

| Grade | No. cases | Pre-menopause | Menorrhagia | | Metrorrhagia | | | Discharge | | Anemia | | | Weight loss | | Pain | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | No. | Per cent of pre-menopausal cases | No. | Duration, months | Per cent | No. | Per cent | Anemic | Not anemic | Per cent anemic | No. | Per cent | No. | Per cent |
| 1 | 57 | 23 | 15 | 65.2 | 48 | 0–12 22<br>13+ 26 | 84.2 | 34 | 59.6 | 15 | 34 | 30.6 | 11 | 19.2 | 16 | 28.1 |
| 2 | 134 | 32 | 16 | 50.0 | 125 | 0–12 80<br>13+ 45 | 93.3 | 101 | 75.4 | 30 | 83 | 26.5 | 33 | 24.6 | 32 | 23.9 |
| 3 | 31 | 7 | 4 | 57.1 | 23 | 0–12 13<br>13+ 10 | 74.2 | 17 | 54.8 | 9 | 19 | 32.1 | 4 | 12.9 | 5 | 16.1 |
| 4 | 35 | 6 | 3 | 50.0 | 28 | 0–12 21<br>13+ 7 | 80.0 | 28 | 80.0 | 8 | 19 | 29.6 | 15 | 42.8 | 8 | 22.8 |

*All recurrent cases are excluded from this table.

different to justify a diagnosis of two primary malignant lesions.

Using the criteria just mentioned, we found in our series the cases falling into the separate stages as follows: stage 1, 89 cases; stage 2, 217 cases; stage 3, 77 cases; stage 4, 84 cases, and 265 unclassified.

*Incidence of leiomyomas.* Leiomyomas occurred in 215, or 36.4 per cent, of 590 cases in which operation was performed. There was no significant difference in percentage of leiomyomas in the less or more extensive lesions.

*Relation of age to extent of lesion.* This is shown briefly in Table III. It can be seen that of stage 1 growths 37 per cent occurred in patients less than 50 years of age; of stage 2, 18.7 per cent; of stage 3, 19.5 per cent; and of stage 4, 24.2 per cent.

*Relation of duration of metrorrhagia to extent of lesion.* Since metrorrhagia is the most significant symptom of carcinoma of the fundus we have used it to designate roughly the duration of symptoms for the successive stages of growth. This is shown in Table IV.

It can be seen that 64.1 per cent of the stage 1 group had either no metrorrhagia or it lasted less than 6 months, and only 24.6 per cent of patients had had this symptom more than 1 year. In the stage 2 group 48 per cent of patients had had no metrorrhagia or it had lasted less than 6 months, whereas 33.2 per cent had had this symptom more than 1 year. In the more advanced lesions the percentage of patients having symptoms for longer periods increases somewhat, although not greatly. Thus stage 3 growths were found with symptoms lasting more than 1 year in 45.5 per cent of cases, and of the stage 4 growths 38.0 per cent had symptoms more than 1 year.

*Relation of anemia to extent of lesion.* Thirty-eight and five-tenths per cent of patients with stage 1 lesions were anemic, 27 per cent of those with stage 2 lesions, 38.8 per cent of those with stage 3 lesions, and 45 per cent of those with stage 4 lesions.

*Relation of anemia to leiomyomas.* Among patients on whom operation was performed and for whom the level of the blood hemoglobin was determined 30.2 per cent of those with leiomyomas were found to be anemic, whereas only 18.3 per cent of the patients without leiomyomas were found to be anemic.

*Relation of menorrhagia to leiomyomas.* Of 205 patients in the premenopausal group on whom operation was performed, 105 had menorrhagia and of these 52 had leiomyomas. Thirty-eight out of 90 patients with leiomyomas did not have menorrhagia, and 53 of 115 patients without leiomyomas had menorrhagia.

*Relation of symptoms to grade of malignancy.* Table V shows that (1) grade 1 of malignancy occurs more commonly before the menopause than do the higher grades; (2) metrorrhagia occurred in 91 per cent of grades 1 and 2, but in only 78.3 per cent of grades 3 and 4; (3) weight loss occurred about twice as frequently in grade 4 lesions as in any other group; and (4) there was no significant difference in the incidence of discharge, anemia, or pain in the lower and higher grades of malignancy. Actually pain occurred slightly more often in patients with grade 1 malignancy than in patients with any of the other grades of malignancy.

TABLE VI.—THE OPERATIVE MORTALITY AND FIVE AND TEN YEAR SURVIVALS ACCORDING TO STAGE OF GROWTH OF CARCINOMA OF THE BODY OF THE UTERUS*

| | Patients operated on up to December 31, 1928 | | | | | | Patients operated on up to December 31, 1933 | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. cases | Hospital mortality | Per cent | No. traced | Alive 5 yrs. | Per cent | No. cases | No. traced | Alive 10 yrs. | Per cent |
| Stage 1 | 89 | 4 | 4.49 | 86 | 72 | 83.7 | 76 | 74 | 52 | 70.3 |
| Stage 2 | 217 | 12 | 5.53 | 210 | 156 | 74.3 | 129 | 121 | 79 | 65.3 |
| Stage 3 | 77 | 6 | 7.79 | 76 | 44 | 57.9 | 52 | 50 | 25 | 50.0 |
| Stage 4, operated on | 49 | 5 | 10.2 | 49 | 12 | 24.5 | 38 | 38 | 4 | 10.5 |
| Stage 4, irradiated | 35 | 0 | 0.0 | 35 | 3 | 8.6 | 27 | 27 | 0 | 0.0 |
| Mixed, operated on | 157 | 10 | 6.4 | 153 | 94 | 61.4 | 140 | 136 | 71 | 52.2 |
| Radiation alone | 67 | 0 | 0.0 | 67 | 32 | 47.8 | 44 | 44 | 12 | 27.3 |
| Radiation, no tissue† | 37 | 1 | 2.7 | 35 | 12 | 34.3 | 31 | 30 | 9 | 30.0 |
| Total | 728 | 38 | 5.22 | 711 | 425 | 59.8 | 537 | 520 | 252 | 48.5 |

*Inquiry as of January 1, 1939.
†This group was largely considered clinically advanced hopeless cases, and no histological diagnosis was established.

TABLE VII.—FIVE YEAR SURVIVALS AND DISTRIBUTION BY GRADE OF MALIGNANCY OF LESION: PATIENTS TREATED BY RADIATION ALONE AND BY OPERATION WITH OR WITHOUT RADIATION

| Treatment | No. cases traced | Survival 5 years | Per cent survival | Per cent of graded cases | | | | Average age, years |
|---|---|---|---|---|---|---|---|---|
| | | | | Grade 1 | Grade 2 | Grade 3 | Grade 4 | |
| Radiation alone | 42 | 25 | 59.5 | 19.0 | 52.4 | 14.3 | 14.3 | 63.4 |
| Operation with or without radiation | 372 | 272 | 73.1 | 26.6 | 55.0 | 10.7 | 7.7 | 55.5 |

SURVIVAL

*Carcinoma of the body of the uterus.* A total of 732 patients suffering from carcinoma arising primarily in the fundus of the uterus was seen at the Mayo Clinic from January 1, 1910, to December 31, 1933, inclusive. Seven hundred twenty-eight of this group were treated, 4 untreated. Five hundred eighty-nine had surgical procedures (with or without irradiation), calculated to remove all or part of the tumor; 139 had some form of radiation exclusively (Table VI).

The hospital mortality for the entire group was 38, with 37 following operative procedures, 1 following radium therapy. In Figure 2 we have graphed the causes of death and the type of procedure in each case. Fourteen deaths were attributed to peritonitis, 12 to pulmonary emboli. Twenty-eight followed total abdominal hysterectomy, 6 followed subtotal abdominal hysterectomy, and 3 followed vaginal hysterectomy. The 1 death in the cases in which irradiation only was used was attributed to coronary occlusion.

The group of 67 cases in which radiation was used alone was made up of cases locally operable and of questionable operability. We have selected 42 cases from this group in which on examination the growth was freely movable, but because of some complicating factor irradiation was employed instead of operative procedures.

In Table VII we have shown the percentage of the various grades in this group treated by irradiation and in the operative groups (including stages 1, 2, and 3) and the 5 year survival.

According to United States life tables, Bureau of the Census, for the years 1929 to 1931, at age 63 the expected mortality in the following 5 years for white females is 14.8 per cent. At age 63.4 in our series of irradiated patients we found 40.5 per cent dead in the next 5 years. Subtracting the 14.8 per cent death expectancy, we found 25.7 per cent dead owing probably to carcinoma of the fundus. At age 55, the average age of our patients on whom operation was performed, according to the United States life tables only 8.1 per cent of white women are expected to die in the following 5 years from all causes. Subtracting this figure from our 26.9 per cent dead in the group of patients upon whom operation was performed we find 18.8 per cent probably dead of cancer.

TABLE VIII.—FIVE YEAR SURVIVALS ACCORDING TO GRADE OF MALIGNANCY AND STAGE OF GROWTH: PATIENTS PRIMARILY TREATED AT THE CLINIC

| | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | | Totals | | Indeterminate | | Per cent alive* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Traced | Alive | Traced | Alive | Traced | Alive | Traced | Alive | Traced | Alive | Traced | Alive | |
| Stage 1 | 15 | 13 | 6 | 6 | 1 | 1 | 1 | 1 | 23 | 21 | 63 | 51 | 83.7 |
| Stage 2 | 29 | 24 | 71 | 50 | 8 | 8 | 7 | 6 | 115 | 88 | 95 | 68 | 74.3 |
| Stage 3 | 1 | 1 | 16 | 8 | 9 | 5 | 5 | 2 | 31 | 16 | 45 | 28 | 57.9 |
| Stage 4, operated on | 5 | 2 | 6 | 2 | 6 | 2 | 7 | 0 | 24 | 6 | 25 | 6 | 24.5 |
| Stage 4, radiation | 0 | 0 | 1 | 0 | 0 | 0 | 5 | 1 | 6 | 1 | 29 | 2 | 8.6 |
| Indeterminate, operated on | 2 | 1 | 15 | 10 | 1 | 0 | 3 | 2 | 21 | 13 | 132 | 81 | 61.4 |
| Indeterminate, radiation | 5 | 3 | 19 | 9 | 6 | 3 | 3 | 1 | 33 | 16 | 69 | 28 | 43.1 |
| Total | 57 | 44 | 134 | 85 | 31 | 19 | 31 | 13 | 253 | 161 | 458 | 264 | |
| Per cent alive 5 years | 77.2 | | 63.4 | | 61.3 | | 41.9 | | 63.6 | | 57.6 | | |

Total average 5 year cure—711 traced cases—60.1 per cent alive.
*Graded + indeterminate.

Although the irradiated group is small, as far as could be determined the 2 groups were both technically operable, and afford as fair a basis of comparison as we were able to get. Probably the death expectancy in the irradiated group is higher than given in the United States life tables since operation was deemed inadvisable because of poor general condition.

In Table VIII we have grouped the survival rates for all traced patients whose lesions were graded and divided into the 4 clinical stages.

There was 1 hospital death in the stage 1, grade 1 group, leaving of the stage 1 graded patients who survived operation only 1 patient dying within the 5 year period.

In Figure 3, we have graphed the percentage of 5 year salvage of all patients traced for whom grading of the tumor was performed and for whom the stage of growth was determined. It can be seen that an early growth implies a slightly better prognosis than a low-grade growth, and that a very extensive growth indicates a graver prognosis than does the grade of the tumor alone.

*Carcinoma of fundus and cervix.* There were 22 patients with malignant lesions in the group, carcinoma of cervix and fundus. Of these, 6 were living 5 or more years and 4 of 21 traced were living 10 years after radiation or operation. Operative procedures, with or without irradiation, were performed on 12; some form of radiation alone was administered to the 10 remaining.

*Carcinoma of fundus and ovary.* Eighteen patients had carcinoma of both uterus and ovary in which the primary site was not definite or in which the possibility of two primary tumors could not be excluded. Sixteen were treated by operative procedures; 2 were treated with radiation alone. Thirteen of the patients on whom operation was performed were alive 5 years after the operation and of 11 patients on whom operation was performed and who were traced 10 years, 7 were alive at the end of that period. Seven of these 18 patients had low grade papillary cystadenoma or grade 1 carcinoma. One of 2 patients treated with irradiation survived 5 years.

The single patient with a fibrosarcoma of the ovary complicating a fundal malignant lesion was alive 6 years following total abdominal hysterectomy with bilateral salpingo-oophorectomy.

*Recurrent carcinoma following treatment elsewhere.* Forty-seven patients had had previous operation or radiation before coming to the clinic. Eight lived 5 years or more after treatment here. Of these 8 surviving patients, only 1 patient had definite tissue diagnosis of carcinoma here. Five patients lived more than 10 years, but in not 1 of these was a definite tissue diagnosis established. One patient came with a large fecal fistula following irradiation and was thought to have a large recurrent pelvic cancer, but lived 9 years and finally died of intestinal obstruction. Two other patients died of carcinoma at the end of 5 and 7 years, respectively.

*Total group of probable carcinoma of the fundus.* Adding these latter groups to our primarily treated series we have 799 patients treated and traced at the clinic for probable carcinoma of the fundus of the uterus with a 5 year salvage of 455

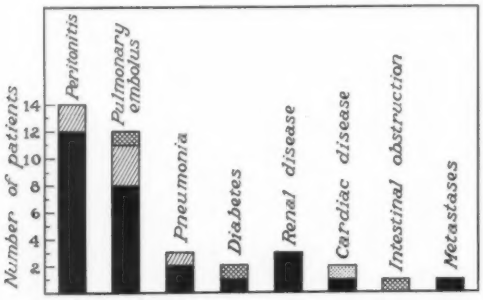


Fig. 2. Frequency of deaths in hospital following surgical and/or radiological treatment for carcinoma of the fundus of the uterus, by cause of death and type of treatment. Black areas, total abdominal hysterectomy; oblique lined area, subtotal abdominal hysterectomy; crosshatched area, vaginal hysterectomy; dotted area, dilatation and curettage and radium.

patients, or 56.9 per cent. Omitting the 47 recurrent cases we find a total of 752 traced primary cases with 447 surviving for a 5 year salvage of 59.4 per cent.

*The influence of leiomyomas on prognosis.* We have traced 210 of 215 patients on whom operation was performed and who had leiomyomas complicating carcinoma of the fundus. Table IX shows the 5 and 10 year survivals for the entire group and for the several stages. These percentages compare quite similarly with all cases of carcinoma of the fundus with and without fibroids (Fig. 3).

*Sarcoma of the uterus.* For comparison we have shown the relative numbers of sarcoma and carcinoma seen at the clinic in the same period together with the 5 year salvage of sarcoma.

TABLE IX.—FIVE AND TEN YEAR SURVIVALS BY STAGE FOR PATIENTS ON WHOM OPERATION WAS PERFORMED AND WHO HAD LEIOMYOMAS COMPLICATING CARCINOMA OF THE FUNDUS

| | 5 years | | | | 10 years | | |
|---|---|---|---|---|---|---|---|
| | No. cases | Traced | Alive | Per cent | Traced | Alive | Per cent |
| Stage 1 | 35 | 35 | 28 | 80.0 | 29 | 21 | 72.4 |
| Stage 2 | 79 | 76 | 54 | 71.1 | 52 | 22 | 42.3 |
| Stage 3 | 24 | 24 | 12 | 50.0 | 21 | 7 | 33.3 |
| Stage 4 | 17 | 17 | 5 | 29.4 | 15 | 1 | 6.7 |
| Unclassified | 60 | 58 | 37 | 63.8 | 55 | 27 | 49.1 |
| Totals | 215 | 210 | 136 | 64.8 | 162 | 78 | 48.1 |

In Figure 4 we have shown the numerical incidence of sarcoma and carcinoma of the fundus by decades. Below the age of 40 years they are of about equal occurrence; from 40 to 49 carcinoma is about 3.5 times as frequent; from 50 to 59 about 17 times as frequent; and from 60 to 69 about 18 times as frequent. Sarcoma did not occur in this series past the age of 70. The ratio of occurrence of carcinoma to sarcoma was 8.8:1.

The 5 year survivals of sarcoma of the uterus according to stage of growth are given in Table X.

Three patients had both adenocarcinoma and sarcoma. In each of these patients the growths had not extended to the serosa and all were living at the end of 5 years. One died after 9 years, cause unknown; the 2 others were living at the last report 6 and 9 years, respectively, after operation.

## EVALUATION

The age of our group approximates that reported by others, as does the marital state and incidence of sterility. About 5 patients were postmenopausal to 2 premenopausal. We were unable to confirm the observation reported by Crossen (4) that menstruation persists longer in women in whom carcinoma of the fundus develops.

The relatively long duration of symptoms before the appearance of the patient for treatment suggests that the malignant lesion is of slow growth or that symptoms are due to other precancerous lesions or associated pathological conditions. The group with fibroids showed no significant difference in menorrhagia, pain, metrorrhagia, or weight loss from those without fibroids but did show a higher percentage of patients with anemia.

A somewhat higher percentage of stage 1 growths was found below the age of 50 years than of the more advanced lesions. That the stage of growth was somewhat indicated by the duration of symptoms is shown in the table for duration of metrorrhagia by stages. In stage 1 growths 64 per cent had had symptoms less than 6 months, whereas in stage 4 growths only 36.9 per cent had had symptoms less than 6 months.

In evaluation of prognosis we have used both the histological grade and extent of lesion. The higher the grade of lesion the more likely it is to be extensive when first seen. Metrorrhagia occurred in about 90 per cent of the grade 1 and 2 cases, and in less than 80 per cent of grade 3 and 4 cases. In all other symptoms there was no significant difference according to grade or extent of lesion.

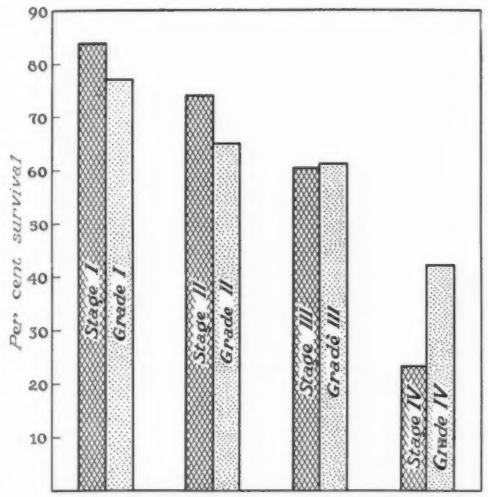


Fig. 3. Comparison of 5 year survival of patients suffering from carcinoma of the body of the uterus according to extent of lesion with survival according to grade of malignancy of lesion.

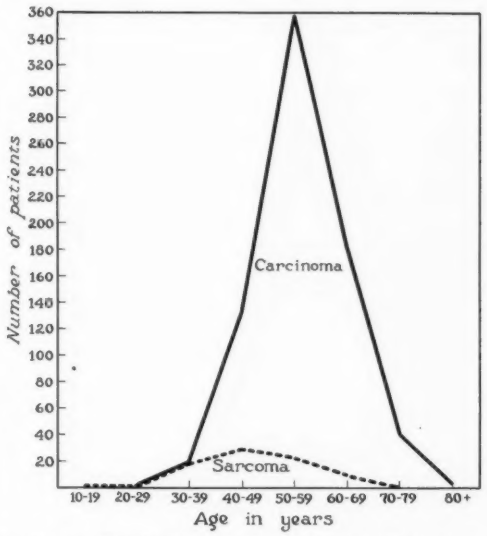


Fig. 4. Distribution by age of patients suffering from carcinoma and from sarcoma of the uterus seen at the Mayo Clinic from January 1, 1910, to December 31, 1932, inclusive.

The operative mortality for cancer of the fundus is about four times that for benign lesions. The mortality rises progressively with the extent of the lesion. Many of the deaths occurred in extensive cancer, but in this group a small percentage lived many years, apparently cured of their malignant lesion. Nearly one-third of the deaths were due to pulmonary emboli.

The gross 5 year survival of the primarily treated group of 59.7 per cent means, deducting 7.5 per cent who would be dead within 5 years after the age of 56 years according to the United States life tables, that approximately 32.8 per cent died of cancer the next 5 years.

The number of patients treated by irradiation alone at the clinic is too small to offer a satisfactory basis of comparison with the results of operation. The 42 cases in which irradiation was used but which were technically operable we have compared with the cases in which operation was performed and in which the malignant lesion had not extended beyond the uterus. This, it seems, is as nearly accurate a basis of comparison as we could get in our series. Heyman, at the Radiumhemmet in Stockholm, has pointed out many of the difficulties in accurately applying radium to fundal cancer. Accurate dosage of roentgen therapy in the very obese is impossible. Phaneuf has calculated that the minimum lethal dose for corpus carcinoma is from 5 to 10 skin erythema units, and that the difficulties of uniform dosage are great. On theoretic grounds alone surgical treatment appears the method of choice in patients with good operative risk. Whether pre-operative irradiation combined with operation gives better results than operation alone will require many years to prove in institutions where large numbers of corpus cancers are treated. In our series the difference in the 5 and 10 year cure after operation with and without irradiation is too small to be of significance.

Whether the stage or grade of growth gives a more accurate estimate of prognosis can hardly be

TABLE X.—FIVE YEAR SURVIVALS BY STAGE FOR PATIENTS SUFFERING FROM SARCOMA OF THE UTERUS

| | No. cases | Traced 5 years | Living 5 years or more | Per cent of traced cases living 5 years or more |
|---|---|---|---|---|
| Stage 1 | 11 | 11 | 7 | 63.6 |
| Stage 2 | 43 | 43 | 32 | 74.4 |
| Stage 3 | 16 | 14 | 3 | 21.4 |
| Stage 4 | 10 | 10 | 2 | 20.0 |
| Unclassified | 4 | 4 | 1 | 25.0 |
| Total | 84 | 82 | 45 | 54.9 |

definitely stated from our series. Of the patients with stage 1 carcinoma, 83.7 per cent were alive 5 years later, regardless of grade, whereas of the patients with grade 1 carcinoma 77.2 per cent were alive 5 years later. In comparing grade 2 malignant lesions with those of stage 2 the prognosis in the stage 2 growths is slightly better than in the grade 2 growths. In the higher grades and more extensive lesions, the higher grade did not give quite as serious a prognosis as the more extensive growth. Significant, however, is the fact that of the stage 4 grade 4 cases in which operation was performed not a single patient was alive 5 years later.

## SUMMARY

The histories of 907 patients suffering from malignant lesions of the body of the uterus seen at the Mayo Clinic from January 1, 1910, to December 31, 1933, inclusive, have been reviewed. Eight hundred eighty were treated and traced 5 years or more. Seven hundred thirty-two patients were seen primarily at the clinic with definite carcinoma of the body of the uterus; 728 were treated. In 22 additional cases there was carcinoma of the body and cervix; in 18 more there was carcinoma of the body of the uterus and of the ovary and in 1 there was carcinoma of the body of the uterus and a fibrosarcoma of the ovary. Forty-seven patients suffering from recurrent carcinoma after treatment elsewhere were seen at the clinic. Three cases of carcinoma and fibrosarcoma in the same specimen were found in the same period. Eighty-four patients suffering from sarcoma were seen in the same period, 82 of whom were traced 5 years or more. An analysis of 732 cases of primary carcinoma of the fundus has been presented in detail.

1. The average age was 56.01 years.

2. Seventy-three patients were single; 659 were married. The average number of children per married woman was 2.21.

3. Two hundred twenty-one patients were premenopausal, 510 postmenopausal. The average age at menopause of the postmenopausal group was 50.27 years, that of a control group 49.9 years.

*4. Symptomatology.* (a) Metrorrhagia was complained of by 660 patients, or 90.2 per cent. Its average duration was 18 months. (b) An abnormal discharge was complained of by 502 patients, or 68.6 per cent. On the average it had persisted 16.4 months. (c) Menorrhagia occurred in 119, or 56.1 per cent of 212 premenopausal patients. It had lasted 49.6 months on the average. (d) Pain occurred in 204 patients, or 27.9 per cent, persisting on the average for 13.2 months. (e) Weight loss occurred in 199 patients, or 27.2 per cent. (f) Of 539 cases in which the level of blood hemoglobin was determined, 199 were anemic.

5. Leiomyomas of the uterus were associated with carcinoma of the fundus in 215 of 590 cases in which operation was performed, or an incidence of 36.4 per cent.

6. Of 257 cases in which the histological grade was determined 57 were graded 1, 134 graded 2, 31 graded 3, and 35 graded 4.

7. In 467 cases which it was possible to classify as to stage of growth, there were 89 stage 1, 217 stage 2, 77 stage 3, and 84 stage 4.

*8. Relation of symptoms to extent of lesion.* Stage 1 patients showed metrorrhagia for less than 6 months in 64 per cent of cases, whereas stage 4 presented metrorrhagia of 6 months' or less duration in only 36.9 per cent of cases.

*9. Relation of symptoms to grade of lesion.* (a) Only 59.6 per cent of grade 1 lesions were postmenopausal, whereas 82.9 per cent of grade 4 lesions occurred in the postmenopausal group. (b) Ninety-one per cent of grade 1 and grade 2 malignant lesions showed metrorrhagia, whereas only 77.3 per cent of grade 3 and 4 carcinomas showed metrorrhagia. (c) Weight loss occurred more frequently in grade 4 lesions than in lesions graded 1, 2, or 3. (d) There was no significant difference in different grades as to discharge, anemia, or pain.

*10. Survival.* (a) The hospital mortality for all treated patients suffering from pure carcinoma of the fundus was 38, or 5.22 per cent. Fourteen deaths were due to peritonitis and 12 to pulmonary emboli. (b) The 5 year survival of 711 traced patients suffering from distinct carcinoma of the fundus was 425 cases, or 59.8 per cent. The 10 year survival of 520 traced patients was 252, or 48.5 per cent. The 5 year survival of all patients having carcinoma of the fundus including those with carcinoma of cervix and ovary was 56.9 per cent. Omitting the recurrent cases, the 5 year salvage was 59.4 per cent. (c) The 5 year survival of 86 traced stage 1 patients was 72, or 83.7 per cent; of 210 traced stage 2 patients, 74.3 per cent; of 76 traced stage 3 patients, 60.5 per cent; and of 49 traced stage 4 patients on whom operation was performed, 24.5 per cent. (d) The 5 year survival of 57 grade 1 traced patients was 77.2 per cent; of 134 grade 2 patients, 64.9 per cent; of 31 grade 3 patients, 61.3 per cent; and of 31 grade 4 patients, 41.9 per cent. (e) Six of 22 patients with carcinoma of the body and also of the cervix lived 5 years after treat-

ment. (f) Of 47 patients with recurrent pelvic carcinoma, probably arising in the body of the uterus, 8 were living 5 years after treatment at the Mayo Clinic.

11. Forty-two patients whose lesions were technically operable but who were irradiated alone because of their poor general condition gave a 5 year salvage of 25, or 59.5 per cent, whereas the 5 year survival of all patients with stage 1, 2, or 3 growths on whom operation was performed was 73.1 per cent. The average age of the irradiated group, however, was 63.4 years, whereas the average age of the group operated upon was 55.5 years.

12. The occurrence of leiomyoma with carcinoma had little influence on the symptoms or prognosis in fundal carcinoma. Anemia was the single factor more common in patients with leiomyoma than in the rest of the group.

13. Eighty-four patients with sarcoma of the uterus were primarily treated at the Mayo Clinic in this period. Eighty-two of this group were traced 5 years. Of them 45, or 54.9 per cent, were living at the end of this period. The hospital mortality was 2 cases, or 2.4 per cent.

14. In 3 cases there were both sarcoma and carcinoma in the same specimen. Each case was in the stage 2 classification, and each patient lived more than 5 years.

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# THE TECHNIQUE OF COMBINED DIVISION, LIGATION, AND INJECTION OF THE INCOMPETENT GREAT SAPHENOUS VEIN

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THE ligation of varicose veins is not a new practice, nor is ligation of the great saphenous vein with injection of its distal portion a new practice. It has been only within the past few years, however, that therapy for varicose veins has been considered satisfactory. This is largely due to improvement of the sclerosing solutions used and better understanding of the principles of ligation. At present, ligation of the great saphenous vein at the saphenofemoral junction, with separate division and ligation of its highest tributaries, together with excision of a small segment of the main trunk distal to the ligature, is considered an essential part of treatment for varicosities in which incompetency of the saphenous system can be demonstrated.

This method has reduced to a minimum the remote danger of embolism. It has increased the ease of subsequent sclerosis due to reduction of gravitational venous pressure. The number of subsequent injections necessary to obliterate completely the incompetent system has been reduced. The chief advantage has been the marked reduction in the incidence of recurrence by elimination of recanalizing influences of the gravitational pressure, by separate division and ligation of all tributaries which might form collateral circulation, and by care to eliminate a blind stump of saphenous vein which might become elongated.

The importance of these points can be better understood by briefly reviewing the anatomy of the great saphenous vein in the region of the fossa ovalis (Fig. 1). The great saphenous vein ends in the femoral vein at the fossa ovalis. Just distal to its junction with the femoral vein there are three comparatively constant tributaries, the superficial circumflex iliac, the superficial epigastric, and the superficial external pudendal veins. These veins, in a few instances, may join directly the femoral vein. At a slightly more distal level, two comparatively inconstant tributaries, the lateral and medial superficial femoral veins, join the great saphenous vein. As a rule, however, these are not visualized in the course of dissection of the great saphenous vein at the fossa ovalis. In approximately 10 per cent of cases in which surgical treatment is employed, a large incompetent vein joins the great saphenous vein at or just distal to the fossa ovalis. This large incompetent vein joins the lateral or anterior aspect of the saphenous vein, lies almost parallel but slightly lateral to the saphenous vein, and is frequently dilated to a size equal to or larger than the great saphenous vein; thus, it can easily be mistaken for the latter. We have called this vessel the accessory saphenous vein, but it is highly probable that this is an incompetent lateral superficial femoral vein that joins the saphenous vein at a level more proximal than is usual (Fig. 1). Its presence can be suspected when a group of varicosities is seen on the lateral or anterior aspect of the thigh. Occasionally, an incompetent medial superficial vein may join the saphenous vein on its anterior or medial aspect at or just distal to the fossa ovalis. When either of these superficial femoral veins is present at this site, it should be dealt with in the same fashion as any other tributary of the great saphenous; in addition, sclerosing solution should be injected into the distal portion.

Our method of combined division, ligation, and injection of the great saphenous vein is similar, in many details, to that proposed by others. Prior to operation, the deep venous circulation is proved adequate, the patient is tested for sensitivity to the sclerosing solution to be employed, and the degree of incompetency of the saphenous vein is determined. Early in our work, we were careful to locate and mark the saphenous vein at the fossa ovalis prior to operation. This was done with the patient standing and by palpating the impulses set in motion along the course of the vein by percussion. When the patient is placed in a supine position with the leg slightly rotated externally, this marking is no longer accurate. Therefore, we have found it more satisfactory to determine the site of the fossa ovalis after the patient has been placed on the operating table and

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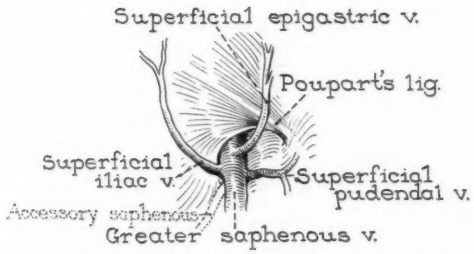


Fig. 1. Great saphenous vein and its tributaries at the fossa ovalis.

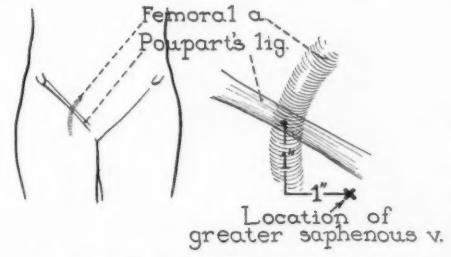


Fig. 2. Method of determining approximate site of fossa ovalis.

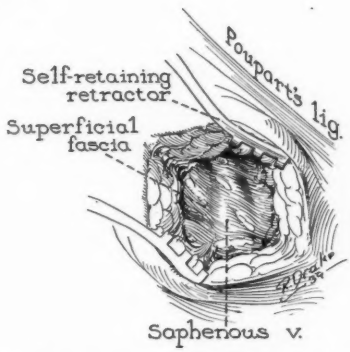


Fig. 3. Incision down to superficial fascia and insertion of self-retaining retractor.

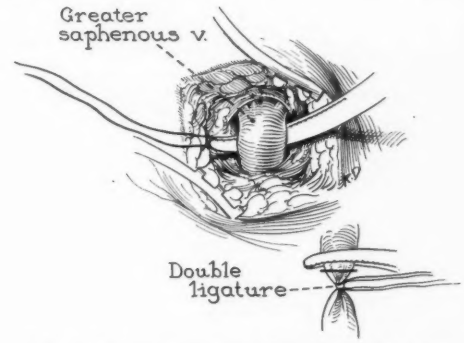


Fig. 4. Great saphenous vein freed from its bed; double ligation of distal portion and site of division of vein are illustrated.

draped for operation. The maximal pulsation of the femoral artery is located at the lower border of Poupart's ligament; by measuring downward approximately 1 inch and then medially approximately 1 inch the saphenous vein has been located satisfactorily at the fossa ovalis in the majority of instances (Fig. 2). A scratch mark is made on the skin at this site. When the vein is large enough, it can be palpated at this site, if the patient produces an increase of intra-abdominal pressure by coughing or straining.

The line of incision and the region immediately above and below are infiltrated with a 1 per cent solution of procaine. Inasmuch as the nerve supply to this field is derived mainly from the outer side, the injection is made first in this region. An ample incision is made parallel to Poupart's ligament, using the marked site of the fossa ovalis as its center. The incision is carried down to the superficial fascia and a self-retaining mastoid type of retractor is inserted (Fig. 3). The operation is greatly facilitated by this permanent and steady form of retraction which does not distort the landmarks. Other additional retraction, when necessary, is obtained by the use of small curved ribbon retractors.

The superficial fascia, which is a continuation of the abdominal Scarpa's fascia, is usually seen as a well defined layer. This definition describes the superficial fascia most characteristic of thin, muscular people; it may be thinned out in obese patients. The great saphenous vein lies beneath this fascia and superficial to the fascia lata of the thigh. This vein frequently can be seen through the superficial fascia which is now picked up and incised in the same direction as the incision. If the vein is not readily visible, it usually may be exposed by blunt dissection by means of a finger covered with a piece of dry gauze to aid in pushing the fat to one side or to the other. The vein is then separated from its bed for a short distance and the curved clamp is passed beneath it (Fig. 4). It is doubly ligated with chromic catgut and a curved clamp is placed on it just proximal to the double ties. The vein is divided between the clamp and ties and the distal portion is allowed to retract downward, being held available by one of the sutures, which has been left long for this purpose.

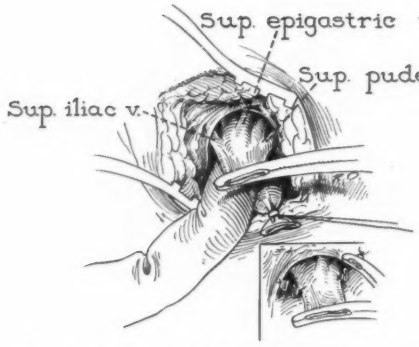


Fig. 5. Dissection of the saphenous vein proximally toward the femoral vein; exposure with separate division and ligation of uppermost tributaries.

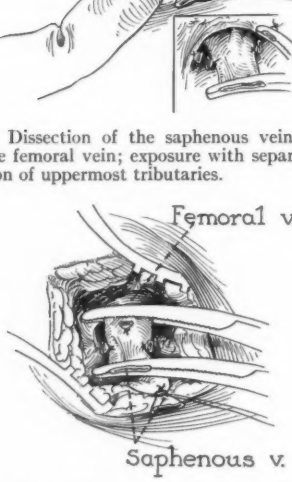


Fig. 6. Clamping of stump of the great saphenous vein at the saphenofemoral junction.

Inasmuch as all of the three uppermost tributaries of the great saphenous vein enter either on the anterior or lateral aspects of the vein, it is now possible to insert the index finger posterior to the proximal stump and carefully strip away the loose areolar tissue that surrounds it, thus exposing it proximally as far as the femoral vein (Fig. 5). This facilitates exposure of the superficial iliac, epigastric, and pudendal tributaries which are divided and ligated separately, and leaves the proximal stump of the great saphenous vein free of any tributaries. Occasionally, the external pudendal artery passes anterior to the saphenous vein and may be divided in order to expose satisfactorily the femoral vein.

By traction on the proximal stump of the saphenous vein, the anterior surface of the femoral vein is exposed and two curved clamps are placed at the saphenofemoral junction (Fig. 6). The great saphenous vein is then doubly tied with chromic catgut sutures just proximal to these clamps. A small stump of vein is left just distal

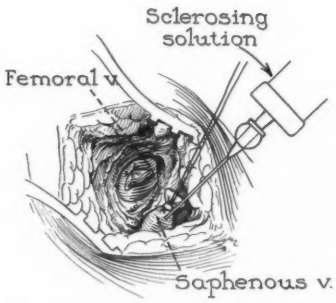


Fig. 7. Ligation at saphenofemoral junction; injection of sclerosing solution into distal portion of vein.

to the second tie and the remainder, usually 3 to 4 centimeters in length, is excised. We have not found it necessary to transfix this doubly ligated stump.

The distal portion of the vein is now pulled into the wound and the sclerosing solution is injected directly into the lumen of the vein (Fig. 7). A needle of small gauge is used so that when tension on the vein is released, the opening in the wall is closed and there is no leakage of sclerosing solution into the surrounding tissues. The wound is irrigated with saline solution and the patient is asked to strain, in order to detect evidence of bleeding. The superficial fascia is approximated by means of two or three interrupted sutures of plain catgut and the skin is closed with interrupted dermal sutures. The patient is allowed to walk to help distribute the sclerosing solution throughout the venous channels, but he is detained in the hospital for a period of 30 minutes or more to observe any untoward reaction that might occur. The patient is allowed to return to his home and to report to the clinic on subsequent days until obliteration of the veins of the lower extremity is completed. None of these patients has experienced a serious reaction following this operative procedure.

It has been our experience that recurrences are dependent, to a great extent, on the thoroughness with which this operation is done. The chances of cure are in direct proportion to the thoroughness and care with which resection of the saphenous veins, together with careful ligation of all communicating branches, is performed. We feel that ligation of the great saphenous vein, with separate division and ligation of its most proximal tributaries, is an essential part of treatment for varicosities in which incompetency of the main saphenous trunk can be demonstrated.

# SIMPLE NON-SPECIFIC ULCER OF THE JEJUNO-ILEUM

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A SIMPLE ulcer of the small intestine is classified as such when it is not due to any of the known etiological agents such as typhoid, dysentery, tuberculosis, syphilis, uremia, gastro-enterostomy, trauma, and tumors; a more descriptive term perhaps is simple non-specific ulcer. This is a relatively rare condition. Only 57 cases, excluding the 2 presented here, have been reported; chiefly in French, British, and Italian literature.

The first comprehensive review of the subject was made by Combes in a thesis at Toulouse in 1897. He stated that the condition was first described by Matthew-Baillie in 1805; and the term simple ulcer was applied by Cruveilhier. Combes described 36 cases, in 7 of which the ulcers were in the jejunum and in 12 in the ileum. Leotta, in 1919, added 13 more cases in 2 of which the ulcers were in the jejunum and in 11 in the ileum. The first recording of any cases in this country was made by Richardson in 1922. He reported 1 case of his own and 1 culled from the records of the Massachusetts General Hospital, the ulcers in both occurring in the jejunum. Since then other cases in this country have been added by Gali, Bigger, Lind, and Brown and Pemberton (5). Brown (4), Babington, Stitch and Collier, and Fellowes have listed cases in the British literature, and Moirond in the French. Of the 57 cases published, in 44 the ulcers were in the ileum and in 13 in the jejunum.

Clinically, the presence of a simple non-specific ulcer is hard to detect. In none of the cases reported was a definite diagnosis made, a perforated ulcer being observed at operation or at postmortem. In 1936, however, Brown and Pemberton (5) reported 9 cases in which operation was performed at the Mayo Clinic for lesions of the small bowel and in which solitary non-perforated ileal ulcers were found. This is the first report of these ulcers being operated upon before perforation occurred.

These ulcers bear a marked resemblance to peptic ulcers (6) in that they may cause intestinal hemorrhage (5), have a tendency to perforate, and histologically show only acute and chronic inflammatory changes.

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The clinical picture presented by these ulcers is varied. The ulcers usually occur in adults who are over 20 years of age, the majority of whom have reached late middle life. They are twice as common in males as in females. Usually there is a history of mild gastro-intestinal distress centered about the umbilicus or, more rarely, of slight intestinal hemorrhage, which may or may not be accompanied by other symptoms. The patient may complain of diarrhea or constipation for a short time prior to the onset of the acute illness. A secondary anemia and occult blood in the stool may be present without any additional symptoms, while all other clinical studies prove negative (5). As a rule, however, the patient is seen because of an acute abdominal condition at the time of perforation when he presents symptoms of acute appendicitis, intestinal obstruction, strangulated hernia, or peritonitis. The outstanding feature at this time, other than the symptoms just mentioned, is that the pain and tenderness are most acute around the umbilicus.

Various theories as to the cause of these ulcers have been presented. Gali thinks they are due to focal infection, citing his case of a woman who had a perforated simple ulcer of the ileum on three separate occasions, each time the condition being preceded by a furunculosis of the auditory canal. Brown (4) also inclines toward the theory of focal infection, citing the work of Rosenow on the selective affinity of certain strains of streptococci for the intestinal tract. Stitch and Collier favor the theory of vascular obstruction, stating that the histological examination in their case showed evidence of endarteritis and thrombosis in some of the vessels of the subperitoneal coat. Taylor (18) and Bigger think that trauma may play a part in this condition. Other authors, as Combes, mention its resemblance to peptic ulcer. The patient observed by us presented evidence histologically of two types of mucosa at the site of the ulcer, which may point to the part played by heterotopic gastric mucosa in the intestinal tract. Several cases of aberrant gastric mucosa in the jejunum and ileum, not associated with a Meckel's diverticulum, have been reported by Kimpton and Crane, Barták, Poindeker, and Taylor (17). Taylor's patient was a 17 months old child who died of intestinal ulceration and

hemorrhage. The specimen obtained at autopsy showed ulceration of gastric mucosa in the ileum. The patient of Kimpton and Crane was a 7 year old girl in whom intussusception was caused by a nodule of gastric mucosa in the jejunum. However, at present, we may safely say that the etiology of this condition has not been established.

These ulcers may vary in size from a pinhead to 2 centimeters. They are punched out in appearance and terraced, the mucosal side being the larger. They may or may not be surrounded by a zone of inflammatory tissue. Usually the remainder of the bowel is normal, although more than one ulcer may be present. Stitch and Collier observed two simultaneous perforations in their patient. Histologically, all show acute and chronic inflammatory changes. These ulcers are three times as common in the ileum as in the jejunum.

When brought to the attention of the physician the treatment is usually surgical, the procedure varying with the pathology found within the abdomen. In 39 patients operated upon, including 1 of our own, resection and anastomosis were performed in 18, with a mortality of 22 per cent. In 15, a simple transverse closure was done, with a mortality of 40 per cent. In 2 cases excision of the ulcer and a transverse closure were carried out, with a mortality of 50 per cent. In 2 cases of simple closure with a short-circuiting anastomosis, the mortality was nil. In 2 cases only drainage of the peritoneal cavity was employed, with 100 per cent mortality. The figures cited are not large enough to warrant drawing definite conclusions, but where possible the procedure of simple closure with a short-circuiting anastomosis to obviate possible stricture of the intestines, seems to be the safest course. In those instances in which the ulcer cannot be closed because of surrounding induration or other causes, resection and anastomosis should be employed. If the perforation is not large a simple closure may suffice. In any event, the simplest procedure compatible with the condition encountered and the future well-being of the patient should be done.

### CASE REPORTS

CASE 1. Mrs. M. K., white, housewife, aged 52 years, was seen at Mercy Hospital on August 13, 1939. She complained of abdominal pain and vomiting of 8 hours' duration. This pain, which began in the lower abdomen around the umbilicus, became progressively more severe and generalized. The patient had two similar attacks a month and a week, respectively, before admission. These were not very severe and were not accompanied by vomiting, and the pain cleared up both times after a saline cathartic. Except for these attacks and the fact that she had no bowel movement for 2 days prior to admission, the patient had been perfectly well.

On admission, the patient's temperature was 100.2 degrees Fahrenheit, pulse 100 per minute, and respirations 28 per minute. The white blood cell count was 7,100 with 96 per cent polymorphonuclear cells. The abdomen was moderately distended with generalized rigidity. Tenderness was present throughout but most marked in the lower abdomen to the right and left of the umbilicus. The patient appeared very ill, presenting a hippocratic facies. A diagnosis of peritonitis, probably due to a perforated viscus or diverticulum, was made. The patient was prepared for operation.

A low midline incision was made and as the abdomen was entered a large amount of cloudy fluid was encountered. On exploration, a loop of ileum about 15 inches from the cecal junction was found folded upon itself and covered with a plastic exudate. In the angle of the fold on the antimesenteric border was seen a perforation, approximately 1.5 centimeters in diameter. It was punched out in appearance, with some induration of the surrounding wall. There was no evidence of the presence of any diverticulum. It was impossible to close this opening because of its size and surrounding induration, so about 4 inches of the bowel was resected and a lateral entero-enterostomy done. The appendix was removed prophylactically because of secondary inflammation of the serosa. The patient had a stormy postoperative period but her temperature and pulse came down gradually until the fourteenth day. At this time after a transfusion, the patient developed an autohemolysis of her blood, jaundice, and anuria, and died on the seventeenth day.

This reaction was later found to be due to the presence of an anti-Z agglutinin in the blood. The presence of this rare agglutinin will be reported and discussed in a separate publication. There was also a question of typhoid in the case because a weak positive agglutination test was reported on the fifth post-operative day. Later agglutination tests were still weaker, all the other tests were negative for typhoid, and the postmortem examination showed no evidence of typhoid.

The histological examination of the resected specimen showed ulceration and perforation with acute and chronic inflammatory changes, and evidence of two types of mucosa.

The postmortem examination showed extensive adhesions over the left upper abdomen. There was about 500 cubic centimeters of bloody fluid around the spleen which was enlarged, friable, and contained numerous infarcts throughout. In the right lower abdomen there was a localized, walled-off abscess of the mesentery due to the opening of the proximal end of the ileum which had been inverted.

CASE 2. (Taken from the records of the Mercy Hospital.) A. J., colored male, aged 20 years, was admitted to the Mercy Hospital on August 29, 1933, complaining of severe generalized abdominal pain of 2 days' duration. The illness began with cramps centered around the umbilicus. These pains became more severe and were accompanied by vomiting. There was no previous history of gastro-intestinal distress or illness of any account, other than constipation for 2 days prior to the onset of the present illness. The patient's condition on admission was precarious, the pulse being 138 and thready, the rectal temperature 101.2 degrees Fahrenheit, and the respirations 34 per minute. The white blood cell count was 9,050 with 81 per cent polymorphonuclear cells. His abdomen was rigid throughout and tenderness was most pronounced in the right upper abdomen. He was treated for shock and peritonitis but died within 24 hours.

The postmortem examination showed an extensive peritonitis and a perforated ulcer, about 1.5 centimeters in diameter, at the middle third of the ileum. The remainder of the ileum was normal.

## SUMMARY AND CONCLUSIONS

To date 57 cases of simple non-specific ulcer of the jejuno-ileum have been reported. This is a relatively rare condition and is difficult to diagnose clinically. It resembles a peptic ulcer in that it may cause bleeding, has a tendency to perforate, and histologically shows acute and chronic inflammatory changes.

The etiology is not definite, but there may be some relation between this condition and the presence of heterotopic gastric mucosa in the small intestine.

Because of the complications produced, surgery is the only treatment; the procedure varies with pathological condition found in abdomen.

Two new cases have been presented and added to the literature.

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# OVARIAN LESIONS SIMULATING APPENDICITIS

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IT has long been recognized that various types of pathological conditions of the female pelvic organs may simulate appendicitis, but comparatively few articles have stressed the frequency with which ruptured follicle or lutein cysts of the ovaries produce symptoms which are mistaken for those of appendicitis. Many of these cases are puzzling and defy accurate pre-operative diagnosis. No question can be raised as to the wisdom of surgical exploration if acute appendicitis cannot be ruled out of consideration at the end of a 36- to 48-hour period of illness; but in the majority of women with ruptured follicle or lutein cysts an accurate diagnosis can be made and the patient spared an unnecessary laparotomy, a procedure to which many women are now subjected.

The first recognition of abnormal hemorrhage from rupture of graafian follicle or corpus luteum cysts appears to have been by Nelaton in 1851, Rokitansky in 1855, and Puech in 1858. According to Phaneuf, the literature previous to 1900 is not clear as to the distinctions between intra-abdominal hemorrhage from these sources and hemorrhages as a result of ruptured extra-uterine pregnancy. The frequency of hemorrhage from ruptured follicles or corpora lutea is a rather recent observation and Odermatt in 1923 was the first to draw attention to the fact that even though only 42 authentic cases had been recorded in the literature up to that date, 1 per cent of female patients operated upon for acute appendicitis had some intra-abdominal hemorrhage not traceable to a ruptured ectopic gestation. In a subsequent investigation on the same subject, Herrmann found 2 patients with corpus luteum hemorrhage among 539 female patients operated upon for chronic appendicitis. From 1930 to 1936, more than 100 authentic case reports have been contributed to the literature. Unlike the survey which we are about to present, the intraperitoneal hemorrhage in most of these patients was so severe that the diagnosis of ruptured ectopic pregnancy rather than appendicitis was the more logical conclusion. In November of 1936, Manizade gathered data on 167 patients with ruptured graafian follicles or corpora lutea whose symptoms were incorrectly diagnosed before operation as acute appendicitis or ruptured tubal pregnancy. All these were confirmed by operation and histological examination. Most of these reports were incomplete with regard to the data on the menstrual cycle, symptomatology, differential diagnosis, etc. In view of the scant attention which this subject has received in medical literature and teaching, it is not at all surprising that the pre-operative diagnosis of ruptured follicle cyst or corpus luteum hemorrhage is seldom made, and some are falsely diagnosed even at operation.

Our study is based on a series of 52 consecutive case histories of patients admitted to various surgical services at St. Bernard's Hospital from January 1, 1933, to December 31, 1938. All of these patients were operated upon with the pre-operative diagnosis of appendicitis, either acute, subacute, chronic, or interval. The histories of these patients are reviewed in an effort to arrive at conclusions that may be of some value in the correct diagnosis and management of similar cases in the future. Cases in which definite appendiceal lesions were found at operation or on microscopic examination are not included. Also not included are those in which a pre-operative diagnosis of some form of adnexal pathology was made. During this same period there were 35,240 patients admitted to the hospital, of which number 8,424, or 23.9 per cent, underwent major surgical operations. Of these, 2,417, or 28.7 per cent, were operated upon with the pre-operative diagnosis of some form of appendicitis. Thus we find that the diagnosis of appendicitis was the indication for operation in over one-fourth of all surgical cases. Table I shows that 75 per cent of these appear to have been correctly diagnosed before operation. In the 25 per cent which remained the diagnosis of appendicitis was either obviously wrong or highly doubtful.

This paper concerns an analysis of the last group shown in Table I. During this 6-year period many women were operated upon with the same pathology but with a pre-operative diagnosis of an ovarian lesion of some type. We have made no attempt to analyze those cases, as the majority of them were diagnosed as "ovarian cysts." It may be noted that these 52 cases represented 3·3 per cent of all of the women in this series of 2,417 patients.

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### PRE-OPERATIVE DATA

In connection with this phase of the problem, the following points have been found to be of significance: the age of the patient, the relation of the symptoms to the menstrual cycle, the social status of the patient, the rôle of trauma in the attack, and the symptoms and findings.

*Age of patient.* Of the 52 patients whom this paper concerns, 11 were between 14 and 20 years of age; 27 between 21 and 30; 12 between 31 and 40; and 2 between 41 and 46. It appears that the climax of frequency is in the third decade. After 35, the curve drops abruptly and no patient older than 46 years was observed. The average age was 25. Manizade reviews in the literature the case histories of 1 patient observed at 10, 1 at 12, and 4 more under 14 years of age.

*Relation of symptoms to the menstrual cycle.* Even though the menstrual period antedating the attack was described as normal in all patients, 40 patients, or 76.5 per cent, complained of pain in the right lower quadrant between the twenty-first and twenty-seventh day after the last menstruation, while 12, or 23.5 per cent, experienced these symptoms on the fourteenth day after the last menstrual period. In the latter group, 8 gave a history of similar attacks for the past 6 or 7 years. Each attack occurred about 2 weeks before the onset of the catamenia and each time recovery occurred without surgical intervention. From these data it might be inferred that the symptoms felt in the mid-intermenstrual time may have resulted from ruptured graafian follicles while those that occurred later may have resulted from ruptured corpora lutea. Ray has reported on 11 patients with ruptured ovarian follicle which produced clinical pictures simulating appendicitis. In all of these patients the attacks appeared between the tenth and fifteenth day after the onset of the last menstrual period. Some degree of bleeding into the peritoneal cavity was found in all of them, and 5 were actively bleeding at the time of operation. This relationship between the menstrual cycle and the onset of the pain naturally suggests the possibility of some ovarian disturbance. It does not necessarily rule out appendicitis for the appendix may become inflamed at any time. Also, the appendix often hangs into the small pelvis, and not infrequently it forms adhesions with the adnexa. In fact, a direct anatomical communication between the ovary and the appendix may exist in the form of ligaments and lymphatics. The former is the infundibulopelvic ligament which may send a cord into the mesoappendix to the right and into the mesosigmoid to the left (7). Thus, by virtue of these anatomical relationships it is possible to explain not only the mechanism of the supposedly "spurious appendicular attacks" associated with menstruation, but also the congestion and even inflammation that may occur in the appendix at the same time that adnexal disease exists, without necessarily postulating the proximity of the two structures. Proof is offered by various authors (13, 15) that excess of secretion of estrin into the graafian follicle at some stage of its development may produce abnormal enlargement to the extent of cyst formation in the ovary. Likewise, failure of the corpus luteum to regress and disappear (in the absence of pregnancy) might result in the formation of an abnormal corpus luteum cyst. While these hormonal influences can explain in some way the mechanism of abnormal rupture of follicle or corpus luteum cysts, the matter of greatest importance is undoubtedly the clinical recognition of the condition. Seventeen of the 58 cases reported by Hoyt and Meigs were diagnosed accurately before the operation. Hence, it is unwarranted to assume that accurate diagnosis is impossible. Rupture of follicle and corpus luteum cysts is probably the most common cause of intra-abdominal hemorrhage, although the great majority of the hemorrhages are mild. No case of severe hemorrhage occurred in this series although many such have been observed by others and to date, the literature reports 7 patients who have died from such hemorrhage.

TABLE I.— PRE-OPERATIVE DIAGNOSIS OF APPENDICITIS, 2,417 CASES

| Postoperative diagnoses— Clinical, pathological or both | Total | Approximate per cent of total |
|---|---|---|
| Acute appendicitis | 915 | 38 } 75 |
| Subacute, chronic, or interval appendicitis | 894 | 37 } |
| Normal appendix and no other pathological condition found | 253 | 10.5 |
| Appendix, normal or abnormal, plus some form of pelvic lesion | 196 | 8.0 |
| Appendix, normal or abnormal, plus some other form of lesion | 107 | 4.5 |
| Normal appendix plus ruptured follicle or lutein cyst of ovary | 52* | 2.0 |

*(These 52 cases were 3.3 per cent of all females in this series)

*Social status.* The evidence indicated that 2 of our patients were virgins. Twenty-one were single and 29, or 56 per cent, were married women. We cannot concur with Krylov's opinion that follicle and corpus luteum hemorrhage are observed only in non-virgins.

*Rôle of trauma in the attack.* In contrast with the reports of other authors (2, 10) that a history of physical exertion such as strain, defecation, sexual excitement, coitus, vaginal examination, dancing, swimming, lifting heavy objects, etc.,

usually precedes the rupture of the corpus luteum or graafian follicle, such data were obtained from only 5 of our patients. This, however, does not disprove the possible rôle of indirect trauma. Kermauner pointed out that there may be a cumulation of various releasing causes. The average interval between the time of physical effort and the onset of the symptoms was about 2 hours in these 5. In 1, the rupture occurred during sleep.

*Symptoms and findings.* With regard to the symptoms and signs, 27 patients had only vague complaints suggestive of appendicitis. In these the abdominal pain was generally first felt low in the abdomen but it was of short duration, or it disappeared and reappeared at intervals, and frequently was felt in different locations. In 25, however, the pain was recorded as being sudden in onset, sharp in character, first generalized over the abdomen and later localized in the right lower quadrant. In 4 of the latter, the pain radiated to the back, and in 1 it was referred to the right shoulder. According to Borras this path of reference is due to a complicated reflex process in the sympathetic plexuses with the arc from the adnexa to the phrenic nerve. Only 2 women complained of fainting. Nausea and vomiting followed the pain in 15 patients, in all of whom the pain had lasted more than 3 hours. On analyzing these symptoms, they were found to be present in those patients in whom pelvic hematomas were discovered at operation. The temperature was recorded as normal in practically all 52, but these were generally mouth temperature readings. Rectal temperatures might have shown different results. The pulse rate showed only slight elevation, and in no case did it exceed 100. The leucocyte count showed a definite increase in the great majority of patients, although the leucocytosis was relative rather than absolute, as shown in cases in which a differential blood count was made. The white blood count in 19 patients was 6,000 to 10,000; in 18 patients, 10,000 to 12,000; in 7 patients, 13,000 to 14,000; in 1 patient, 19,000; and in 4 patients, 22,000 to 23,400. The average count was 10,500; 2 had 6,000. Urinalysis was essentially negative in all cases.

Unfortunately, findings on rectal and vaginal examinations were recorded in the histories of only 4 patients; in 2 of these patients a doughy fullness suggestive of an accumulation of blood or blood clots was felt in the cul-de-sac. Vaginal examinations on others were done previous to admission to the hospital but the findings were not recorded. Most of these cysts are too small to be diagnosed as such by bimanual palpation, but definite ovarian tenderness, if elicited, is of value in the differentiation of them from appendicitis. Abdominal tenderness was elicited in all patients, the maximum degree usually being somewhat medial to and below McBurney's point and nearer the symphysis pubis. However, the point of maximum tenderness in appendicitis may be in an atypical site (1). In 5 patients the tenderness shifted to the upper quadrant. Rigidity and muscle spasm were not a constant finding; neither was increased peristalsis on auscultation of the abdomen.

### OPERATIVE DATA

None of these patients had had a previous laparotomy performed. A right rectus incision was made in all cases. Twenty-four surgeons performed the operations. One surgeon had 6 patients; 3 others had 5 each; 3 had 4 each; 2 had 2 each; and 15 other surgeons had 1 each. Unlike the data in many reported cases, free blood was found when the peritoneal cavity was opened in only 2 patients of this series. Thirteen had what might be considered moderate hemorrhage in the pelvis. In 24 the bleeding was very slight and seemed to come from a pin-point area on the right ovary. The left ovary was involved in only 2 patients, although the symptoms in these were localized entirely on the right side. In 3 other patients observed by one of us (C.C.G.) in other hospitals, the pain and tenderness were entirely in the right lower quadrant but the ruptured cyst in each was in the left ovary. We can advance no satisfactory explanation for this paradox. Of the 11 patients whose histories are reported by Ray, the right ovary was involved in 7 and the left ovary in 4. He comments on the predominance of pain and tenderness on the right side even in those patients in whom the lesion was located in the left ovary, but he attempts to make no explanation of this observation. In 11 of our patients there was no evidence of active oozing, the condition having been discovered during the process of pelvic exploration after an apparently innocent appendix had been removed. A clear serous or blood-tinged fluid was found in the pelvis in these, probably the result of ruptures of graafian follicles. According to Novak the amount of hemorrhage depends largely on the location of the rupture of the cyst structures in relation to its blood vessels. A rupture in a relatively avascular area produces very little bleeding. Plastic resection of the hemorrhagic cyst alone was done on 12 patients. Twenty-nine were treated by partial oophorectomy and 11 others by total unilateral oophorectomy. Two of the latter were the 2 patients over 40 years of age. Simple suture of the bleeding tissue was not done. In 40 patients, or

76.5 per cent, the pathological diagnosis was hemorrhage from corpus luteum cyst. Twelve, or 23.5 per cent, appeared to be ruptured graafian follicles. The excised ovaries showed edema and fibrocystic changes but no true inflammatory reactions were found. In 2 there was diffuse follicle cyst formation. None showed histological evidence of pregnancy thus disproving Forssner's contention. Appendectomy was performed on all patients. Gross and microscopic examination of all of these appendices failed to reveal pathological changes which appeared sufficient to produce symptoms. Incidentally, in 15 women of the series normal menstruation appeared on the third postoperative day. All recovered uneventfully.

### PHYSIOPATHOLOGICAL ASPECTS

Physiological rupture of a graafian follicle and the formation of a corpus luteum (ovulation) is thought to occur usually between the twelfth and nineteenth day before the onset of the period. Any disturbance in the process of follicular ripening from hormonal, traumatic, or other causes may result in a pathological rupture with extravasation of clear white to yellow coagulated fluid and sometimes actual hemorrhage. The severity of the symptoms depends to a large extent on the amount of intraperitoneal bleeding that occurs with the rupture. In most instances it is of little consequence. The pain that results from it resembles "gas" pain, it rarely incapacitates the patient and seldom lasts more than 3 hours. It is in the exceptional case in which the hemorrhage is diffuse, and this symptom can easily be confused with that of ruptured tubal pregnancy. Yet, a thorough menstrual history, especially in women whose catamenia are regular, is helpful in the differential diagnosis. Thus, if the symptoms occur between the twelfth and the nineteenth day after the last menstruation, they may be due to rupture of the graafian follicle while the more pronounced abdominal symptoms which are likely to occur 7 to 10 days before the onset of the next period may be due to rupture of corpus luteum cysts. Previous similar attacks are very suggestive but, unfortunately, a history of previous attacks is also frequent in appendicitis, the disease with which it is most often confused. The argument, therefore, is not so much against the removal of an innocent appendix, but for the realization of the fact that after appendectomy, with or without the performance of oophorectomy, the symptoms may recur; and if one ovary has already been removed, the reproductive and endocrine functions of the patient are needlessly impaired. Consequently, the opinion that a ruptured corpus luteum or graafian follicle cyst is invariably a surgical problem is not shared by the authors. It seems questionable to expect that the great majority of these women will be permanently benefited by operation. If an accurate diagnosis is made and mild attacks recur, endocrine therapy may be of value (5).

### SUMMARY

1. Rupture of follicle and corpus luteum cysts may simulate a surgical condition of the abdomen. This is not rare, since the histories of 52 patients whose symptoms were erroneously diagnosed as appendicitis have been gathered and studied in a 6-year period from a 200 bed hospital.

2. The relation of the time of onset of the symptoms to the menstrual cycle is found to be of major diagnostic importance.

3. About one-half of the patients experienced sudden pain in the lower abdomen at the onset. This is a second important diagnostic sign.

4. Vaginal or rectal examination may be helpful in the diagnosis and should always be done.

5. In most of the patients the symptoms experienced are mild, can be correctly diagnosed, and spontaneous recovery can be expected. In other patients, the symptoms and clinical findings are more pronounced and may so closely simulate appendicitis, tubal pregnancy, or other pelvic lesions that surgical exploration is advisable.

6. If operation is performed, every effort should be made to conserve the maximum amount of ovarian tissue.

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# EDITORIALS

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## PROSTATIC SURGERY

FOR some obscure reason the treatment of the obstruction to urination due to disease of the prostate gland has long been the subject of lively controversy. It arose first between the proponents of operation on the one hand and those of catheterization on the other. The former triumphed when it proved that in the long run catheterization had the higher mortality. Then came the quarrel between the perineal and the suprapubic operators. Its echoes were still resounding when such hardy pioneers as Caulk, Davis, Bumpus, and Alcock raised the question of transurethral resection, and the debate, which is still in progress, became three cornered and increased in intensity.

Several factors contribute to the current disagreement as to the selection of the proper operation for a given case of prostatism. Suprapubic prostatectomy is the more widely used of the open operations because it is easy to perform and carries almost no risk of incontinence. Its high mortality and long, often unpleasantly moist convalescence have been potent arguments for the adoption of transurethral resection.

Perineal prostatectomy is difficult to master but has a low mortality. The very real and definite danger of urinary incontinence and recto-urethral fistulas which accompany its use have prevented its widespread adoption and have, to some extent, promoted acceptance of the endoscopic operation. It also is likely to be followed by a long, damp, malodorous recovery.

Many instruments and operations for transurethral removal of the prostate were tried and discarded as dangerous and futile in the second half of the nineteenth century, especially by Guthrie, Civiale, Mercier, Bottini, and Wishard. Although Young described the successful use of his punch as early as 1911, he employed it only in contractures of the prostate, and it was not until about ten years ago that Caulk first succeeded in convincing others that prostatic hypertrophy was amenable to operation by endoscopic methods. Shortly thereafter, some of his early followers greatly underestimated the seriousness of the procedure and reported, very prematurely indeed, that it was so free from risk that it could be done "in the office"; many who were encouraged by such reports were so speedily and violently disillusioned by their own experiences as to abandon it forever.

Another definite obstacle to the widespread adoption of the operation is the fact that its successful performance requires a wide experience, first with the cystoscope, and later with the resectoscope, with an opportunity to begin with the smaller glands and, as experience

increases, very gradually to attack the larger ones. Opportunities for the acquisition of such experience are difficult to find.

Habit has also served to prevent wider employment of the transurethral operation. This was well expressed by the surgeon who asked, "Why is it that, just when I learned to do a decent prostatectomy, someone had to change the rules?"

The fact that even a well conducted transurethral resection leaves a certain amount of abnormal tissue behind cannot be denied; the danger that this will give rise to recurrent obstruction has been advanced as a reason for abandoning the operation in hypertrophy of the prostate. Before doing so, one must remember that hypertrophy develops so slowly, and the average patient is so old, that death from other, unrelated causes is likely to precede recurrence. It is not amiss to point out that the literature contains many instances of recurrence following enucleation of hypertrophies from patients who lived unusually long after operation.

Another objection, advanced particularly by Young, is based upon the incontrovertible fact that transurethral resection cannot cure a prostatic cancer concealed in a spheroid of benign hypertrophy, while enucleation or radical perineal prostatectomy may do so. The fact is, as I have pointed out, that such a small number of prostatic cancers are curable by any means at the time of their discovery—one to three per cent—that the lower mortality of transurethral resection entirely compensates for the lost cures.

It has also been suggested that urinary incontinence has become so frequent as a result of the employment of the transurethral operation as to constitute a windfall for manufacturers of incontinence clamps and bags. It has apparently not occurred to many who cite this fact that the frequent occurrence of incontinence is a reflection upon the operator rather than upon the operation.

Notwithstanding these conflicting ideas, certain facts concerning the merits of the transurethral operation are well established. First, the expert can, if he chooses, resect all but the monstrous enlargements of the gland, although the resection of the larger ones is tedious for patient and surgeon alike and may require multiple stages.

Second, a potent factor in the adoption of transurethral resection has been its low mortality in skillful hands. Caulk, Davis, Thompson, and others have reported large series of cases with a mortality of one-half to one per cent. While it is perfectly true that the average surgeon cannot achieve such results, it is equally true that the mortality of two to three per cent reported by Young and Davis after perineal prostatectomy, and that of 5.4 per cent by Hunt after the suprapubic operation cannot be equalled by the average operator. Nevertheless, the ratio of 1:3:5.5 probably represents the relative risk of the three operations well performed for proper indications.

A third point in favor of the transurethral route is that it requires a relatively short hospital stay, Thompson having been able to dismiss two-thirds of his cases after 5 to 7 days; a fair average for the pre-operative and post-operative stay is ten to fourteen days. Open operation, on the other hand, is likely to require four weeks or more of hospitalization although some patients are able to leave earlier.

Fourth, the transurethral operation achieves an enormous saving in discomfort and post-operative care by eliminating the "wet period" and the need for dressings.

Bearing these facts in mind, one may draw up a tentative set of rules, always subject to modification, for the selection of the proper operation in a given case of prostatism.

The general surgeon should avoid the transurethral operation entirely unless he has had an unusual training, and has a large proportion of urological patients, since it is as much a specialist's operation as is trigeminal rhizotomy. Whether the general surgeon elects the suprapubic or perineal route for open operation is a matter of personal preference although it must be understood that, while the perineal route has a lower mortality, its use by surgeons without special training is fraught with disturbing possibilities of incontinence and recto-urethral fistulas. Undoubtedly the best operation for the general surgeon is the two stage suprapubic, in which he employs a technique of cystostomy which minimizes trauma and allows ample time for full recovery before he performs a blind intraurethral enucleation and packs the prostatic cavity. In this way he avoids such pitfalls as primary closure.

Safe guides for the selection of the individual case are somewhat as follows:

Prostatic fibroses are amenable only to transurethral resection, since they cannot be enucleated.

The obstruction of prostatic carcinoma with local extension or metastasis is most easily and safely relieved by an endoscopic operation. Localized carcinoma may be cured by radical perineal prostatectomy, an operation which can be done well by but few surgeons.

Small hypertrophies are best treated by resection although they can be removed, at somewhat greater risk and expense, by the open method.

Large hypertrophies are best treated with suprapubic prostatectomy except in the hands of the expert in the perineum. It must be remembered that the term "large" is relative since one surgeon may be quite capable of removing more than a hundred grams of prostatic tissue quickly and safely by the transurethral route, while another may exhaust both the patient and himself in removing more than ten or fifteen grams of tissue.

While this scheme of treatment may arouse the objection that it requires referring the majority of patients to the specialist, this objection is not valid if one considers the welfare of the patient which is, after all, the surgeon's primary objective.

C. D. Creevy.

## THE PROPER USE OF THE TERM "CANCER"

IT is unfortunate that the term *cancer* should so often be interpreted in a limited sense as applying to malignant tumors of epithelial origin only, i.e. carcinoma. There is need for a definite term, a single word, to define the general group of malignant neoplasms—carcinoma, sarcoma, endothelioma, myeloma, melanoma, etc., collectively—and there is none available except "cancer," which originally had this broad meaning. The necessity for the broad conception of this term is proved by its frequent use in that sense in the lay and medical press. In most foreign languages, the word is not used in its limited sense.

Synonyms are "malignant tumor," "malignant growth," "malignant neoplasm."

The term *malignancy* is an abstract noun meaning "the state or quality of being malignant; the tendency to a fatal issue; the tendency to go from bad to worse. The term "malignancy" therefore is one of the qualities or characteristics of cancer and also of a number of other diseases. There is no authority for using it as a concrete noun and a synonym for cancer. When improperly used, the error should be corrected by substituting the term "cancer" or one of its synonyms as given above.

The clearest (abstract) meaning of this term will in most cases require the addition of the preposition "of," as for instance in speaking of "the malignancy of a growth" or of any given disease. Although it may of course be correctly used as an abstract noun standing alone, nevertheless, the omission of the preposition "of" is apt to lead to errors in construction.

The term *malignant disease* designates any disease which tends to go from bad to worse or which tends to a fatal issue. It is obvious that from the quantitative standpoint, the most malignant disease therefore is that which causes the most deaths, that is, that ill-assorted collection known as "heart disease." Cancer comes second from this standpoint. From the qualitative standpoint, cancer can often be cured, while many diseases, as for example, tetanus, are almost always fatal, and lastly, many diseases cause death more quickly than cancer, as for instance, septic endocarditis or typhus. It is obvious, therefore, that the term "malignant disease" is ill-chosen and improper when used as a synonym for cancer.

The terms *carcinoma* and *epithelioma* refer exclusively to growths of epithelial origin, which are admittedly the most frequent of malignant tumors. Nevertheless, connective tissue tumors (sarcomas) may occur in any organ or part of the body, and the title of a general paper on any of these subjects necessitates the use of the word "cancer" or one of its synonyms. The title "carcinoma of the breast" excludes by inference any connective tissue tumor of the breast, which is usually not intended, and furthermore is both unnecessary and unwise.

The terms "carcinoma" and "epithelioma" are best reserved for the discussion of the histological type of cancer and usually had best be accompanied by a qualifying prefix or adjective, as for instance, "squamous carcinoma," "adenocarcinoma," "lympho-epithelioma," etc. In the majority of instances when the word "carcinoma" alone is used in medical writing without further qualification, the meaning would be made clearer if the word "cancer" or one of its synonyms were substituted for it.

The old anatomies speak of *lymph glands*—a term which arose at the time when lymph nodes were considered as secretory organs. At the present time, their true function is known, and there is no longer any justification for calling them "glands"—a practice which leads to some confusion. For instance, when lymph nodes of the neck are called "glands of the neck" or "cervical glands," the less clear thinking and less well informed physician is often erroneously led to believe that metastasis takes place indiscriminately to the true glandular structures of the neck which are the parotid salivary gland, the submaxillary salivary gland, the sublingual gland and the thyroid gland.

While there is less confusion as regards the lymph nodes of the axillæ, groins, and such regions, good practice calls for the use of "axillary lymph nodes," rather than "axillary lymph glands." In medical journals, the elimination of the use of the term "glands" in referring to lymph nodes would soon correct the present day tendency, which is so widely prevalent, to commit this error.

HAYES MARTIN.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

JOHN Homans has long written authoritatively on circulatory diseases of the extremities. The advent of his monograph[1] on the subject, therefore, could not fail to arouse interest. In contrast with other numerous recent publications in this field, his volume covers disturbances of all of the component systems of the peripheral circulation, including diseases of the arteries and veins, abnormal arteriovenous communications, and obstructions to the lymphatic return. The book is well balanced and well written. It is restrained and scientific in tone and thoroughly fulfills the high standard expected of it.

The work is primarily intended for the general practitioner who is first called upon to recognize and treat disorders of the peripheral circulation. In the section on arterial diseases, therefore, emphasis is placed upon diagnostic tests and therapeutic methods generally available and requiring no unusual apparatus or equipment. On the other hand, the critical evaluation of recent contributions and the description and illustration of operative procedures should be of interest to the surgeon particularly concerned with vascular disturbances. There is a notable reserve toward certain therapeutic measures that contrasts with the enthusiastic reports of other writers. In addition to the usual chapters devoted to arteriosclerosis and thrombo-angiitis obliterans, there is an interesting grouping of the numerous diverse, and little understood ischemic conditions under the general heading of spastic arterial states, with particular attention to their presumed reflex origin and to methods of interrupting the pathological reflex cycles.

The author speaks with greatest conviction when discussing disturbances of the veins, a study to which he has made notable contributions. Consonant with his earlier views, he is still rather restrained in his attitude toward the injection treatment of varicose veins and considers it, at best, an adjuvant to properly placed ligations of the venous trunks. Surgical excision of varicosities finds wider indications than in most current writings on the subject. The chapter on thrombophlebitis and pulmonary embolism encompasses his extensive observations on this phase of vein disease and is, therefore, one of the most valuable in the book.

Case reports and adequate illustrations enhance the clarity of the presentation. A selected bibliography is appended to each chapter. In general, this is the most satisfying monograph on the subject of circulatory diseases that has appeared in recent years. It should prove of interest and value to all who treat these conditions, and this, of course, includes almost all who practice medicine or surgery.

LEO M. ZIMMERMAN.

IN the second edition of his book, *Blood Groups and Blood Transfusion*,[2] Dr. Wiener has reviewed the recently accumulated knowledge concerning blood groups, subgroups, sources of error in blood grouping, the use of preserved blood for transfusion, blood transfusion reactions, medicolegal aspects of blood groups, and differences in animal blood.

The section on the history of blood transfusion is the only division not revised in this new edition. Particularly valuable is the greatly enlarged chapter on blood transfusion reactions which includes much recently published material not previously available outside of current periodicals. In his discussion of methods the author has given no consideration to the simple closed citrate transfusion apparatus which is being used successfully in hospitals and large clinics.

The monograph offers in a readily available form all the information necessary for the carrying out of a complete blood transfusion. No hospital laboratory should be without access to this book and it can be recommended particularly to those young men in our hospitals who are performing the majority of blood transfusions.

THOMAS C. DOUGLASS.

THE author of *Tumors of the Skin*[3] has been deeply interested for years in the study of neoplasms and in order to obtain information on various phases of the subject he frequently found it necessary to consult many sources. For this reason he felt that there was a need for a single comprehensive and practical volume on the diagnosis and treatment of benign and malignant tumors of the skin.

The book is not a large one but covers the most important details of benign and malignant neoplasms of the skin. Under benign tumors are discussed tumors of connective tissue origin, tumors originating from muscle or nerve tissue, nevi, and other developmental disturbances of the skin, tumors of infectious origin, and precancerous conditions. Malignant tumors are treated as carcinomas, malignant melanomas, sarcomas, and lymphomas. The volume contains brief but adequate descriptions of all of the neoplasms, supplemented with excellent photographs, both clinical and microscopic. Treatment is adequately given at the end of each subject.

[1] CIRCULATORY DISEASES OF THE EXTREMITIES. By John Homans, M.D. New York: The Macmillan Co., 1939.

[2] BLOOD GROUPS AND BLOOD TRANSFUSION. By Alexander S. Wiener, A.B., M.D. 2d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1939.

[3] TUMORS OF THE SKIN; BENIGN AND MALIGNANT. By Joseph Jordan Eller, M.D. Philadelphia: Lea & Febiger, 1939.

There is an excellent chapter on cutaneous surgery and plastic repair of skin tumors which discusses in detail various types of incisions, closures, indications for the various kinds of skin grafting, and the technique used for them. Finally, there is an appendix containing practical data on radiation, physics, and biology. In addition there are dosage tables and charts which are useful in determining the proper procedure and dose to be employed.

While the author discusses his own technique in the use of roentgen rays and radium in the treatment of cancer, he makes it plain that good results may also be obtained with different techniques and dosages. One of the few criticisms that can be made of this excellent work is that in some instances the dosage suggested may not be excessive in the hands of an experienced operator like the author, but in less experienced hands such dosages may prove to be dangerous. The average physician will have difficulty in understanding the various dosage tables in the appendix. While these are undoubtedly readily understood by the expert radiologist, it would seem best to interject some explanatory text for the benefit of the average practitioner.

A special feature of the book in the chapter on carcinoma, and an excellent one, is a series of diagrams of tumors of various types, sizes, and locations, with a practical discussion of the different methods of therapy which may be used for each lesion.

Every subject is well organized and at the end of each chapter is an extensive bibliography. The text reads smoothly and the illustrations are numerous and excellent. Seldom does one see such a large number of uniformly choice illustrations. The print is large and legible and the author and publishers are to be most earnestly congratulated for producing such a fine volume. EDWARD A. OLIVER.

THE present volume[1] of *Transactions of the Third International Goiter Conference and the American Association for the Study of Goiter* contains 61 papers on thyroid disease. Kimball reviews "Twenty Years in the Prevention of Goiter." He says, "The incidence of goiter among the school children of Cleveland in 1924 was 31 per cent." In this community, however, the prevention of goiter and especially the generalized use of iodized salt had been frankly and repeatedly criticized by some well known surgeons. There was such a widespread fear of the so called "dangers of iodized salt," that less than one-half of the homes in Cleveland ever used it. In 1936 a resurvey showed the total incidence of goiter to be 18.5 per cent. Among those using iodized salt regularly it was 7.7 per cent, and among those not using it at all the incidence was 30.7 per cent, or practically the same as in 1924. He concludes: "The addition of an exceedingly small amount of iodine to our food (one part sodium iodide to ten thousand parts of salt) in endemic goiter regions prevents goiter. There is no basis for the old teaching that the general use of iodine in amounts sufficient to prevent goiter might have some injurious effects. In the prevention of endemic goiter we prevent adenomas and toxic goiters, cretinism and cretinoid type of subnormal mentality, deaf-mutism, congenital malformations and many cases of infantilism in girls or a relative subnormal development." Similar enthusiastic reports are given by Eggenberger and Messerli from Switzerland. Other papers from Mexico, Finland, Poland, and Russia discuss goitrogenic factors.

The 6 papers in the next section are concerned with thyroid disease in childhood. The fourth section contains 5 papers on tumors of the thyroid. The fifth section is concerned with the endocrine physiology of the thyroid. The sixth section is surgical, the seventh, medical, the eighth is a symposium on iodine metabolism with important papers by Curtis, McClendon, Perkin, Litchfield, and Webster; the ninth section concerns the vitamins and the thyroid; the tenth has several experimental papers; the eleventh is composed of 3 papers on basal metabolism. The volume closes with a paper on x-ray therapy and one on colloid goiter.

In general, this volume contains very valuable material on every phase of thyroid physiology and disease. PAUL STARR.

FROM the long experience of a large surgical practice there has evolved the practical book on ophthalmic surgery, *Surgery of the Eye*,[2] by Wiener and Alvis. No claim is made that it constitutes an exhaustive treatise on all known techniques and methods, but the authors have attempted to present in detail the operative procedures which in their hands have proved to be most effective. For this reason some rather widely used forms of ophthalmic operations and technical modifications are omitted from the text. Some surgeons may disagree with the choice of operations in some instances but such disparity of views is unavoidable in a text as personal in nature as the present one.

The classical description of dacryocystectomy found in Meller's widely utilized book has been used as a model in describing operative stages. For the most part operations are described in a lucid, explicit, and detailed manner, and only occasionally does the language become sufficiently involved to require a rereading. The greatest asset of the book and its most commendable feature is the complete and intelligent manner in which it is illustrated. The 396 drawings were sketched and then finished by Dr. A. J. Hofsommer, an artist who is also a medical graduate. They are accurate and comprehensible, and serve to clarify descriptions which would otherwise, by their very nature, be difficult for the novice to comprehend correctly.

Separate chapters are devoted to: (1) general considerations; (2) preparation of the patient; (3)

[1] TRANSACTIONS OF THE THIRD INTERNATIONAL GOITER CONFERENCE AND THE AMERICAN ASSOCIATION FOR THE STUDY OF GOITER. 1938 Joint Meeting, Washington, D. C. Portland, Oregon: The Western Journal of Surgery, Obstetrics and Gynecology, 1939.

[2] SURGERY OF THE EYE. By Meyer Wiener, M.D., and Bennett Y. Alvis, M.D. Philadelphia and London: W. B. Saunders Co., 1939.

anesthesia; (4) pre-operative preparation; (5) post-operative care; (6) paracentesis; (7) cataract; (8) glaucoma; (9) operations on the retina and sclera; (10) intra-ocular foreign bodies; (11) operations on the cornea; (12) removal of the eye; (13) operations on the conjunctiva; (14) operations on the lids and socket; (15) ptosis; (16) muscle operations; (17) operations on the tear apparatus.

There have been in the past few acceptable textbooks on ophthalmic surgery written in the English language. Therefore, the present effort is a welcome addition to the ophthalmic surgeon's library.

WILLIAM A. MANN.

A TEXTBOOK of surgical anatomy may be either primarily clinical or anatomical; it may teach procedure and merely employ the facts of gross anatomy in supportive capacity, or may emphasize anatomical structure while presenting surgical concepts as general corollaries. The *Manual of Surgical Anatomy*[1] belongs definitely in the latter category. The descriptions are primarily anatomical, arranged in the regular order of successive stratification. For example, in presentation of the surgical anatomy of the head, palpable bony landmarks are first described, next the skin and its regional peculiarities, then the subcutaneous tissue and the latter's vascular content, the epicranial aponeurosis, the pericranial periosteum, the skull, and finally the brain and meninges. Appropriately placed are the comments on the surgical importance of each layer: the mobility of sebaceous cysts, the limitation of hemorrhage by the density of the superficial fascia, viability of torn flaps as dependent upon richness of blood supply, the broad spread of hemorrhagic or purulent masses when situated beneath the aponeurosis of the cranial muscles, intersutural restriction of similar collections when they lie beneath the pericranium, the bilaminar structure of cranial bones in relation to fractures, the spread of infection from ear and mastoid to the venous sinuses, and the anatomically advantageous position for sampling the cerebrospinal fluid.

The extremities are similarly treated. For example, in the discussion of the upper extremity, the muscular and bony prominences are first described, then the course of superficial nerves, and the areas to which pain is referred from thoracic, phrenic or subphrenic pathology, the scheme of superficial venous drainage and the sites of hematoma, the course of the arteries with points of convenient ligation, the joints, ligaments, and surrounding muscles in relation to the common positions of dislocations; the routes of lymphatic drainage, and the synovial sheaths with relation to spreading tendovaginitis.

Of the descriptions of the several serous cavities, that of the abdomen may be selected as an example. The peritoneum is discussed with detailed commentary on the spread of infections within the sac, the natural control of such conditions by the great omentum, and the sites for incision in drainage of purulent masses. The separate portions of the digestive tube are described fully as they appear in the living patient, in the cadaver, and in roentgenograms; the lymphatic drainage of each organ is presented in relation to malignant involvements; and the physiological features affecting resection are discussed.

More than one-fourth of the 187 figures in the book are used in either Cunningham's *Manual* or Cunningham's *Textbook*, or in both of these. Most of the new figures are radiographs, which had been added in the previous edition and repeated in the current one; roentgenograms, in fact, make up almost one-fifth of the total number of figures in the volume. Some figures on developmental anatomy are presented; they are conventionally diagrammatic. Normal variation is sparingly handled; there are figures only of the modes of termination of the biliary and pancreatic ducts, of the degrees of persistence of the vitello-intestinal duct, and of the varying relation of the cecum and ascending colon to the peritoneum. Vascular variations of surgical importance are neglected.

Relatively few of the figures are surgical. Unlike the plan followed in a recently revised American textbook of surgical anatomy, the Beesly and Johnston edition does not illustrate successive steps in the exposure, repair or excision, and closure of surgically important structures. Figures which may be regarded as surgical at all are fundamentally topographical; they illustrate cistern puncture, sites of alveolar abscess, route of approach in malignancy of the tongue, lines of incision in the hand and the abdominal wall, and types of hernial sac.

The volume is very readable and the arrangement of its subject matter admirable; it gives the impression of completeness and carries an air of quiet authoritativeness. The book is a corpulent octavo of more than 700 pages which would fit handily into the larger pocket of a mackintosh. BARRY ANSON.

THE text of Professor Clark's *Tissues of the Body*,[2] which is designed to present in modern fashion the structural organization of the living body, the dynamic bases of human anatomy, opens with a general discussion of cells and tissues. A concise account of technical methods follows describing such procedures as dissection, histological technique, reconstruction from serial sections, tissue culture, and vital staining. A serviceable chapter is devoted to the development of tissues in the embryo. Although form is of first importance to the anatomist, no mention is made of the shape of cells in layers, so ready is histology to espouse chemistry when its natural allies are the physical sciences.

In the discussion of connective tissue the account is not unlike that found in any one of the American

[1] BEESLY AND JOHNSTON'S MANUAL OF SURGICAL ANATOMY. 5th ed. Revised by John Bruce, M.B., F.R.C.S.(Edin.), and Robert Walmsley, M.D. London: Oxford University Press, 1939.

[2] THE TISSUES OF THE BODY; AN INTRODUCTION TO THE STUDY OF ANATOMY. By W. E. LeGros Clark, F.R.S. Oxford: Clarendon Press, 1939.

textbooks of histology. The treatment of the macrophage system is illuminating and gives a serviceable concept of its broad distribution within the body in connective tissue, liver, lymph glands, leptomeninges, and central nervous system. Similarly helpful to the student is the proper placement of superficial and deep fascial layers in the scheme of supporting tissues.

Cartilage receives scant attention, as is regularly the case in textbooks, and often in the larger edited works. Bone, on the contrary, is dealt with at some length in a most able fashion: all phases are considered from comparative anatomy, through development, to surgical significance of the periosteum. A simple account of ossification is followed by an appraisal of features controversial in nature. All the mechanics of bony architecture, the factors influencing the initiation of ossification, and the ultimate shape of bones receive attention.

In the section on skeletal muscle, not only is the structure of the myofibril considered, but the organization of the fibrils into named muscles of various forms: fusiform, flat, penniform, etc. The physiological principles governing contraction, the atavistic variations in the muscular system and retrogressive changes of higher mammals, and the regeneration and repair of muscle tissue are also discussed. Visceral and cardiac types are more briefly treated. Some lost causes are given passing note, as for example, the "double innervation" of skeletal muscle, and, in this way, are given decent textual interment.

On the subject of blood vessels the new concepts regarding endothelial growth are presented, as are also thoseconcerning the establishment of embryonic vascular patterns and the mode of innervation of blood vessels. This is done without disregarding the more conventional material. On the subject of lymphatic capillaries the important recent work on direct observation of the living vessels is both described and figured.

Mucous membranes and their glands are discussed, first in the ordinary way, then with consideration of special features: the macroscopic features of glands, to relate gross to microscopic appearance; the anatomy of secretion, to correlate cytological elements with histological appearance; the embryology of secretion, to relate the adult position and form of the glandular masses to the manner of their embryonic formation.

To the more conventional discussion of the skin is added a consideration of flexure lines, racial variation in pigmentation, hair tracts, and hair growth.

The volume closes with a section on the tissues of the nervous system. The general account is enlivened by a discussion of the differentiation of neural mechanisms and the evolution of nervous organization. An explanation of methods of studying experimental and clinical material is appended.

Professor Clark's treatise is energizing and diverting. It is very well written and the subject matter is judiciously selected. Since it is the work of a single author, the presentation is even, the parts nicely correlated; one encounters none of the irritating disjunction, irregularity of treatment, and lack of integration which characterizes the more pretentious histologies produced under editorship. Just the optimum number of references is given. The photomicrographs are excellent.

The book could not be used by a student in an American medical school as a substitute for his regular textbook of histology, but it would form a highly valuable addition to his library. For the graduate in medicine its usefulness would be even greater.

BARRY ANSON.

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# BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

SYNOPSIS OF OBSTETRICS. By Jennings C. Litzenberg, M.D., F.A.C.S. St. Louis: The C. V. Mosby Co., 1940.

PATOGENIA DE LA HIDATIDOSIS BI-EPIFISARIA DE LAS ARTICULACIONES. By P. Larghero Ybarz. Montevideo: A. Monteverde & Cia, 1939.

GRADUATE MEDICAL EDUCATION IN UNITED STATES for 1937 to 1940. Chicago: American Medical Ass., 1940.

TOMORROW'S CHILDREN. Proceedings First Southern Conference Atlanta, Ga., November 9–11, 1939. New York: Birth Control Federation of America, 1940.

MODERN MEDICAL THERAPY IN GENERAL PRACTICE. Edited by David Preswick Barr, A. B., M.D., LL.D. Vol. 1—GENERAL THERAPY, METHODS USED IN THERAPY, GENERAL DISEASES. Vol. 2—INFECTIOUS DISEASES, DISEASES OF THE NERVOUS SYSTEM, DISEASES OF THE DIGESTIVE SYSTEM. Vol. 3—DISEASES OF OTHER ORGANS AND SYSTEMS, GENERAL INDEX. Baltimore: The Williams & Wilkins Co., 1940.

TREATMENT OF CANCER AND ALLIED DISEASES. By 147 International Authors. Edited by George T. Pack, B.Sc., M.D., and Edward M. Livingston, B.Sc., M.D. Vols. 1, 2, 3. New York and London: Paul B. Hoeber, Inc., 1940.

SPECIALTIES IN MEDICAL PRACTICE. Edited by Edgar Van Nuys Allen, M.D. Vols. 1 and 2. New York and Edinburgh: Thomas Nelson & Sons, 1940.

OXFORD MEDICAL PUBLICATIONS. AN INTRODUCTION TO MEDICAL GENETICS. By J. A. Fraser Roberts, M.A., M.B., D.Sc., F.R.S.E. London: Oxford University Press, 1940.

OXFORD MEDICAL PUBLICATIONS. A TEXT-BOOK OF PSYCHIATRY. By D. K. Henderson, M.D. (Edin.), F.R.F.P.S. (Glas.), F.R.C.P.E., and R. D. Gillespie, M.D.(Glas.), F.R.C.P.(Lond.), D.P.M.(Lond.). 5th ed. London: Oxford University Press, 1940.

OXFORD MEDICAL PUBLICATIONS. THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE PERIPHERAL ARTERIES. By Saul S. Samuels, A.M., M.D. 2d ed. London, New York, Toronto: Oxford University Press, 1940.

THE EARLY DIAGNOSIS OF THE ACUTE ABDOMEN. By Zachary Cope, B.A., M.D., M.S.(Lond.), F.R.C.S.(Eng.). 8th ed. London: Oxford University Press, 1940.

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

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JOHN A. WOLFER, *Chairman;* CHARLES B. PUESTOW, *Secretary*

## PRELIMINARY PROGRAM FOR 1940 CLINICAL CONGRESS

THE thirtieth annual Clinical Congress of the American College of Surgeons will be held in Chicago, October 21 to 25, when surgeons of this medical center plan to present a program of operative clinics and demonstrations covering all phases of the clinical activities of the five medical schools and forty or more participating hospitals. Representing as it does the interests of all surgical specialists as well as general surgeons, this Clinical Congress, under the leadership of a strong and representative committee, will assure a complete and varied program for all those who will attend. The five day program will include a presentation of the latest advances in diagnostic methods, surgical technique and operative procedures, and the after care of the surgical patient. A preliminary schedule of the clinical programs at a number of the hospitals and medical schools, prepared at the direction of the committee, appears in the following pages. Other hospitals that will participate in the Clinical Congress are: Children's Memorial, Evangelical, Grant, Illinois Central, Loretto, Municipal Contagious Disease, Ravenswood, Shriner's Hospital for Crippled Children, United States Marine. Clinics and demonstrations will be held on the afternoon of Monday, October 21, and the mornings and afternoons of each of the succeeding four days.

### CLINICAL PROGRAM

The committee is arranging an extensive schedule of operative clinics in which the technique of a wide variety of surgical procedures will be demonstrated in the operating rooms. The program is being planned, in so far as possible, so that it will also cover related problems in diagnosis, pre- and postoperative care, and other special aspects of the management of the surgical condition under consideration.

EXECUTIVE COMMITTEE

| | |
|---|---|
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A series of non-operative clinics, demonstrations, and exhibits is planned in many of the larger hospitals for the presentation of important work being done in many special fields. The program of each hospital and medical school is arranged to cover subjects in general surgery, obstetrics and gynecology, fractures and other traumas, thoracic surgery, neurosurgery, urology, orthopedic surgery, and ophthalmology and otolaryngology. Presentations of subjects under these classifications are being so correlated that the visiting surgeon will have the opportunity to devote his time continuously to clinics dealing with the specialty in which he is most interested. The daily clinical bulletin will present the program according to the above classification in order to facilitate the selection of clinics which the visiting surgeon desires to attend. The complete detailed clinical program for the succeeding day will be posted each afternoon in the form of bulletins at headquarters in the Stevens Hotel and distributed in printed form each morning.

### SCIENTIFIC SESSIONS

The opening scientific session of the Clinical Congress will be held on Monday evening in the ballroom of the Stevens Hotel, when the Presidential Meeting and Convocation will be combined. The new officers of the College will be

inaugurated and the initiates received into fellowship. Distinguished surgeons from foreign countries will then be introduced, following which Dr. George P. Muller, of Philadelphia, will deliver the presidential address.

Scientific meetings will be held on Tuesday, Wednesday, and Thursday evenings at headquarters, and outstanding members of the profession, of national and international prominence, will address the assembled guests of the Congress. The speakers and subjects of these addresses are being carefully selected to assure contributions which will be of interest to those practicing in all of the special fields of surgery. As in former years, separate scientific meetings are being arranged for Tuesday and Thursday evenings for the presentation of papers on subjects of special interest to the ophthalmologists and the otolaryngologists, by surgeons who are outstanding in these fields.

Panel discussions have met with such decided success at the Clinical Congress and sectional meetings of the College, that the schedule this year will include thirty or more such conferences arranged for Monday, Tuesday, Wednesday, and Thursday afternoons. Recognized authorities are co-operating with the College as leaders and collaborators of these panels and a careful selection of topics will cover pertinent subjects in all fields of surgery. This program will permit more informal discussion of these subjects than would be permitted in larger general meetings. The plan provides that the leader will present his subject within a ten-minute period, collaborators will then discuss various phases of these topics briefly, after which general discussion from the floor will be encouraged.

Important features of the afternoon sessions at headquarters are: (1) Symposium on fractures and other traumas; (2) symposium on cancer; (3) conference on graduate training for surgery.

A new feature of considerable interest to all surgeons attending the Congress will be a series of group clinical conferences which are being arranged for Friday afternoon. Ten special fields of surgery have been selected and a pertinent subject of current interest will be briefly presented in each conference. Leaders will then direct discussions from the floor and any surgeon attending the meeting will be invited to present a special problem with which he is concerned—one that is related to the special field under discussion. Recognized authorities will endeavor to answer these questions and offer as much helpful advice as possible. Everyone should benefit by participating in a consultation conference of this nature.

The Board of Regents plans to provide a varied scientific program for the 1940 Clinical Congress that will appeal to all general surgeons and also offer to those interested in the surgical specialties an opportunity to learn of the newer developments in their respective fields.

### GRADUATE TRAINING IN SURGERY

The College program for graduate training in surgery will receive special attention at the Congress. There will be a session devoted to a program on this important subject which should elicit the interest of all hospital executives as well as surgeons and educators who are concerned with the future standard of surgery in the United States and Canada. Authorities will present a brief program dealing with various types of educational programs, following which there will be a general discussion from the floor. All visitors to the Congress are invited to participate in these discussions.

### MEDICAL MOTION PICTURES

An enlarged program of surgical motion pictures will be presented at headquarters which will include the latest available films on a wide variety of subjects of interest to the surgeon. The schedule will be arranged so as not to conflict with either the clinical program at the hospitals or the scientific sessions and will include both sound and silent, standard and color films which have been approved by the Committee on Medical Motion Pictures.

### HOSPITAL CONFERENCE

The twenty-second annual Hospital Standardization Conference will open the Clinical Congress with a meeting at headquarters on Monday morning at 10:00 a.m. Official announcement of the 1940 approval lists of the College which deal with hospital activities will be made at this meeting. Throughout the week there will be a series of hospital meetings with practical demonstrations, panel discussions, and round table conferences, dealing with all phases of hospital administration and various problems related to management, efficiency and education in the hospital. One hospital conference will be devoted exclusively to subjects of vital interest to hospital executives and members of governing boards. At a joint session with the Association of Record Librarians of North America, the subject of medical records will receive special consideration from the standpoint of their relationship to the clinical work of the physician, and the medical and surgical specialist. There will be ample opportunity

during the Congress for visitors to inspect the hospitals in Chicago and vicinity.

### PUBLICATION OF PROCEEDINGS

As in former years, the formal papers which are presented at the scientific sessions of the Congress will be published in a special issue of the official journal of the College, SURGERY, GYNECOLOGY, AND OBSTETRICS, in February following the meeting. This is furnished without additional charge to all Fellows, junior candidates, and others who register for the Congress as invited guests. The papers which are presented in connection with the Hospital Standardization Conference are published in subsequent issues of the *Bulletin* of the American College of Surgeons.

### ADVANCE REGISTRATION

The hospitals and medical schools of the Chicago area afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the clinics. The limit of attendance will be based on a survey determining the available facilities in the participating hospitals and schools. It is expected, therefore, that surgeons who wish to attend the Congress will register in advance. A registration fee will be required in order to provide funds with which to meet expenses of the meeting. A formal receipt will be issued to each surgeon registering in advance which will be exchanged for a general admission card upon presentation at headquarters during the Congress. This card, which is not transferable, must accompany all requests for clinic tickets and be presented for admission to the scientific sessions.

A resolution adopted by the Board of Regents provides that the registration fee for Fellows of the College and endorsed junior candidates shall be $5.00; that no fee for the 1940 Clinical Congress shall be required of initiates (class of 1940); that the fee for surgeons who are not Fellows, attending as invited guests of the College, shall be $10.00.

As in previous years, admission to clinics and demonstrations in the hospitals and certain of the scientific meetings at headquarters will be controlled by means of tickets. This plan provides for the distribution of visiting surgeons at the various clinics and other meetings and helps to insure against overcrowding. The number of tickets issued for any clinic will be limited to the capacity of the room in which the clinic is held. Visiting surgeons are urged to co-operate in making the clinic ticket plan a success.

### HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Stevens Hotel where there are unusual facilities for accommodating the Congress. All of the public rooms have been reserved for conferences, registration, ticket bureaus, clinic bulletins, executive offices and scientific exhibits. Thus, all activities of the Congress, except the clinical program, will be located under one roof.

The technical exhibition together with the registration desk will be located on the lower floor of the Stevens Hotel in the large exhibition hall. Leading manufacturers of surgical instruments and supplies, sutures, dressings, pharmaceuticals, operating room equipment, x-ray apparatus and hospital equipment of all kinds, as well as publishers of medical books will be represented in the exhibition. It will provide for the visiting surgeons an opportunity of carefully inspecting the finest modern products of all those industries which are aiding the work of the surgeon and the hospital.

### CHICAGO HOTELS AND THEIR RATES

In addition to the headquarters hotel, the Stevens, there are several first-class hotels within short walking distance of headquarters, providing ample hotel facilities at reasonable rates. It is suggested that reservation of hotel accommodations be made at an early date. The following hotels are recommended by the Committee:

| | Minimum Rate with Bath | |
|---|---|---|
| | Single | Double |
| Auditorium, 430 S. Michigan Ave. | $2.50 | $4.00 |
| Bismarck, 171 W. Randolph St. | 3.50 | 5.00 |
| Blackstone, Michigan Ave. at 7th St. | 4.00 | 6.00 |
| Congress, 500 S. Michigan Ave. | 3.00 | 5.00 |
| Drake, Michigan and Lake Shore Drive | 4.00 | 6.00 |
| Harrison, 57 E. Harrison St. | 2.00 | 3.00 |
| LaSalle, 10 N. LaSalle St. | 2.50 | 4.00 |
| Morrison, 79 W. Madison St. | 2.50 | 4.00 |
| Palmer House, 15 E. Monroe St. | 3.50 | 5.00 |
| Sherman, 106 W. Randolph St. | 2.50 | 4.00 |
| Stevens, 720 S. Michigan Ave. | 3.00 | 4.50 |

# PRELIMINARY CLINICAL PROGRAM

## COOK COUNTY HOSPITAL

### *Monday*

OBSTETRICS AND GYNECOLOGY

A. J. KOBAK and H. H. HILL—2. Studies in acriflavine and glycerine.
JAMES H. BLOOMFIELD—2. Demonstration of cases: Cesarean section and local anesthesia, or management of occiput posterior.
S. J. BENENSOHN—2. Lues in the prenatal clinic.
T. J. MORRIS—2. Puerperal infection.

FRACTURES AND OTHER TRAUMAS

WILLIAM R. CUBBINS, J. J. CALLAHAN and C. S. SCUDERI—1. Operative clinic.

### *Tuesday*

GENERAL SURGERY

KARL A. MEYER—9. Operative clinic: Stomach and colon.
JOHN R. HARGER—9. Operative clinic: Peridural anesthesia for major operations.
C. C. GUY—9. Dry clinic: Surgical problems in the diabetic.
SUMNER L. KOCH—9. Dry clinic: Injuries and infections of the hand.
RAYMOND W. MCNEALY—10. Operative clinic: Gall bladder; gastric surgery.
E. M. MILLER—10. Dry clinic: Bowel obstruction in the newborn; gangrene complicating scarlet fever; volvulus of sigmoid colon in children.
J. D. KOUCKY—10. Operative and dry clinic: Arteriosclerotic gangrene of the legs.
JOHN B. O'DONOGHUE—10. Operative clinic: Gastrointestinal.

OBSTETRICS AND GYNECOLOGY

W. T. CARLISLE—9. Gynecological operations.
A. E. KANTER—10. Gynecological operations.

ORTHOPEDIC SURGERY

ARTHUR CONLEY and DONALD MILLER—9. Operative clinic.
MARCUS H. HOBART and FELIX JANSEY—10. Operative clinic: Shoulder injuries.

THORACIC SURGERY

JEROME HEAD—10. Dry clinic.
R. B. BETTMAN—2. Operative clinic.

OTOLARYNGOLOGY

JACOB LIFSCHUTZ—2. Operative and dry clinic.
RAYMOND W. KERWIN—2. Operative and dry clinic.

### *Wednesday*

GENERAL SURGERY

VICTOR L. SCHRAGER—9. Operations.
HAROLD C. VORIS—9. Dry clinic: Operative treatment of head injuries.
RALPH C. SULLIVAN—9. Operations.
EDWARD A. CHRISTOFFERSON—9. Operative clinic: Appendicitis.
FRANK J. JIRKA—10. Dry clinic: Dysgerminoma in the male.
J. R. BUCHBINDER—1. Operative clinic: Thyroid; biliary tract.

OBSTETRICS AND GYNECOLOGY

HERBERT E. SCHMITZ—9. Gynecological operations.
A. F. LASH—10. Gynecological operations.

FRACTURES AND OTHER TRAUMAS

GEORGE L. APPELBACH—2. Operative clinic: Flange operation for fractured neck of femur; open reduction of the forearm with intramedullary peg; reconstruction of malunited Colles' fracture.

ORTHOPEDIC SURGERY

PHILIP LEWIN and SIDNEY SIDEMAN—9. Operative clinic.
DANIEL H. LEVINTHAL and staff—9. Dry clinic.

OPHTHALMOLOGY

JAMES E. LEBENSOHN and WILLIAM F. MONCREIFF—9. Operations.

OTOLARYNGOLOGY

S. J. PEARLMAN—10. Operative and dry clinic.
JACOB LIFSCHUTZ—2. Operative and dry clinic.

### *Thursday*

GENERAL SURGERY

RALPH C. SULLIVAN—9. Operative clinic.
MARSHALL DAVISON—10. Operative clinic: Thyroid.
RALPH B. BETTMAN—2. Operative clinic.

OBSTETRICS AND GYNECOLOGY

E. W. FISCHMANN—9. Gynecological operations.
J. P. GREENHILL—10. Gynecological operations.

FRACTURES AND OTHER TRAUMAS

WILLIAM R. CUBBINS and JAMES J. CALLAHAN—1. Operations.

ORTHOPEDIC SURGERY

FRANK G. MURPHY and WALTER FISCHER—9. Operations.
E. J. BERKHEISER—10. Operations.
ARTHUR H. CONLEY and staff—10. Dry clinic.

OTOLARYNGOLOGY

RAYMOND W. KERWIN—2. Operative and dry clinic.

### *Friday*

GENERAL SURGERY

LOUIS RIVER—9. Dry clinic: Abdominal incisions.
E. H. WARZEWSKI—10. Operative clinic: Reconstruction treatment of burns.
J. R. BUCHBINDER—1. Operative clinic: Gastric resection for duodenal ulcer.

OBSTETRICS AND GYNECOLOGY

WILLIAM H. BROWNE—9. Gynecological operations.
FREDERICK H. FALLS—10. Gynecological operations.
AUGUST DARO. Use of epinephrine in acute inversion of the uterus.

LOUIS RUDOLPH. Ring dystocia constriction.
JAMES E. FITZGERALD. Heart disease in pregnancy.
DAVID S. HILLIS. Recognition of cephalopelvic disproportion.
AUGUSTA WEBSTER. Vitamin K in pregnancy.

ORTHOPEDIC SURGERY

FRED HARK and CLAUDE LAMBERT—9. Operations.
H. KELIKIAN and GRAHAM A. KERNWEIN—10. Operations.

OPHTHALMOLOGY

SANFORD R. GIFFORD—9. Operations.
EDWARD A. ROLING—10. Operations.

OTOLARYNGOLOGY

JACOB LIFSCHUTZ, T. C. GALLOWAY, and R. W. KERWIN—10. Operative and dry clinic.

*Days to be Announced*

GENITO-URINARY SURGERY

HARRY CULVER, HARRY C. ROLNICK, D. F. RUDNICK, and L. L. VESEEN. Operations.

## RESEARCH AND EDUCATIONAL HOSPITALS

*Wednesday*

GENERAL SURGERY

W. H. COLE—9. Thyroidectomy.
P. W. GREELEY—9. Plastic surgery.

OBSTETRICS AND GYNECOLOGY

FREDERICK H. FALLS and staff—1. Vaginal hysterectomy; cesarean section.

GENITO-URINARY SURGERY

C. H. MCKENNA—9. Operations.

NEUROSURGERY

ERIC OLDBERG, PERCIVAL BAILEY, W. A. GUSTAFSON, and MILTON TINSLEY—9. Operative and dry clinic.

*Thursday*

GENERAL SURGERY

CHARLES B. PUESTOW—9. Cholecystectomy.
R. B. MALCOLM—9. Radical mastectomy.

ORTHOPEDIC SURGERY

H. B. THOMAS, F. W. HARK, C. N. LAMBERT, and P. H. DUBE—1. Hip joint surgery and end-results: Fracture of neck of femur; epiphyseal separations.

OPHTHALMOLOGY

HALLARD BEARD and staff—9. Operative and dry clinic.

OTOLARYNGOLOGY

F. L. LEDERER and staff—9. Operative and dry clinic.

## HENROTIN HOSPITAL

*Wednesday*

GENITO-URINARY SURGERY

C. O. MILLER—9. Neoplasm of the kidneys.

FRACTURES AND OTHER TRAUMAS

RALPH A. KORDENAT—9. Operations.
JOHN A. GRAHAM—9. Demonstration, with lantern slides: Fracture of distal end of radius.

## ST. LUKE'S HOSPITAL

*Tuesday*

GENERAL SURGERY

W. R. CUBBINS—9. Operations.
GEZÁ DE TAKATS—9. Operative clinic: Lumbar sympathectomy.
SELIM W. MCARTHUR—9. Operations.
Staff—9. Dry clinic:
E. C. HOLMBLAD and R. A. JACOBSON. Treatment of gas gangrene.
T. L. HANSEN and DR. JENSEN. Shelf fractures of tibia.
JOHN ELLIS. Amputations.
G. V. PONTIUS. Hypertrophic pyloric stenosis in the adult.
GEZÁ DE TAKATS and J. T. REYNOLDS. Indications and results of sympathectomy in Buerger's disease.
H. I. MEYER. Paget's disease; osteitis deformans.

OPHTHALMOLOGY

ELMER VORISEK—2. Demonstration of cases.

*Wednesday*

GENERAL SURGERY

PAUL GREELEY—9. Operative clinic: Plastic surgery.
H. E. MOCK—9. Operations.
Staff—9. Dry clinic:
SELIM W. MCARTHUR. Stomach deformities simulating malignancy in their x-ray study.
F. L. MCMILLAN. Lesions of the colon.
H. E. MOCK. Breast tumors; malignancies and granulomas of the gastro-intestinal tract; pancreatitis.
H. E. JONES. Treatment of complete biliary fistulas.
E. LEE STROHL. Common duct obstructions.
W. G. DIFFENBAUGH. Autoplastic operation for hernial repair; statistical report.

ORTHOPEDIC SURGERY

HENRY B. THOMAS—9. Bone changes in connection with thyroid disease.
FRED W. HARK—9. Bone changes in connection with sickle-cell anemia.
CLAUDE N. LAMBERT—9. Bone tumors.
HARRY E. MOCK, ALVIN R. MORROW, CHARLES E. SHANNON, JOHN L. LINDQUIST, and DONNELL C. HOWE—10. Operative and dry clinics: Conservative treatment of fractures of neck of the femur; supracondylar fractures of humerus; malunited fractures of the ankle.
JOHN D. ELLIS—10. Compression fractures of vertebræ using Ryerson hyperextension device.
EDWIN W. RYERSON—1:30. Operative clinic: Shelf operation at the hip; reconstruction of hip joint; osteotomy to produce back-knee.
FREMONT A. CHANDLER—2. Operative clinic: Aseptic necrosis of head of femur.
ROBERT E. RITTER—2:30. Arthroplasty.
HAROLD A. SOFIELD—3. Discussion of leg lengthening operations; indications and technique.
Open forum—3:30.

*Thursday*

OBSTETRICS AND GYNECOLOGY

Staff—9. Operations.

GENITO-URINARY SURGERY

L. E. SCHMIDT and staff—9. Operative and dry clinic.

OPHTHALMOLOGY

E. V. L. BROWN—9. Demonstration of cases.
FRANK BRAWLEY and JAMES W. CLARK—2. Demonstration of cases.

*Friday*

OPHTHALMOLOGY

RICHARD GAMBLE—3. Demonstration of cases.

*Days to be Announced*

FRACTURES AND OTHER TRAUMAS

H. E. MOCK and staff. Skull fractures.
W. R. CUBBINS. Abdominal injuries.
ERIC OLDBERG. Spinal injuries.
GEZÁ DE TAKATS. Circulation and trauma.
E. W. RYERSON. Conservative treatment of fractures.
HAROLD SOFIELD. Fractures of the femoral neck.
P. W. GREELEY. Plastic repair of cutaneous defects.
T. P. GRAUER. Injuries of the genito-urinary tract.
A. P. SOLOMON. The psychic aspect of injuries.

OTOLARYNGOLOGY

HORACE R. LYONS, WALTER H. THEOBALD and staff—1. Operative and dry clinic: Sulfanilamide therapy in acute mastoiditis and acute otitis media; Proetz treatment for sinusitis.
PAUL H. HOLINGER and ALBERT H. ANDREWS, JR.—2. Peroral endoscopy; clinical presentation of bronchial and esophageal cases.

## MERCY HOSPITAL

*Days to be Announced*

GENERAL SURGERY

M. MCGUIRE—9. Operative and dry clinic: Biliary tract.
L. D. MOORHEAD—9. Operative and dry clinic: Thyroid.
WILLIAM PICKETT—9. Operative and dry clinic: Gastric surgery.
C. F. SAWYER—9. Intestinal obstruction.
J. SANDROY and JOHN SHEEHAN—9. Tests for liver function.
A. K. VAUGHN—9. Treatment of varicose veins and ulcers.

OBSTETRICS AND GYNECOLOGY

HERBERT SCHMITZ and staff—9. Operative and dry clinic: Vaginal hysterectomy; Watkins transposition operation; Manchester-Fothergill operation for vaginal plastic; anterior colporrhaphy and perineorrhaphy; LaForte colpocleisis.

GENITO-URINARY SURGERY

H. E. LANDES—9. Clinical cystometry, an aid in the diagnosis of disturbances of micturition.

NEUROSURGERY

HAROLD C. VORIS—9. Dry clinic: Protruding intervertebral disc.

OPHTHALMOLOGY

CARL SCHAUB and L. G. HOFFMAN—9. Operative and dry clinic. Demonstration of verified cases of opticochiasmatic arachnoiditis.

OTOLARYNGOLOGY

PETER P. LEDERMANN—9. Disturbances of equilibrium.
CARL CHRISTOPH—9. Laryngeal malignancies.
HERBERT NASH—9. Endaural operations.
G. T. JORDAN—9. Anatomy of the temporal bone.

## MICHAEL REESE HOSPITAL

*Monday*

GENERAL SURGERY

JAMES PATEJDL. Gastro-intestinal operations.
ALFRED A. STRAUSS and SIEGFRIED STRAUSS. Gastro-intestinal operations.
Staff. Operative and dry clinics: Gastro-intestinal surgery; faciomaxillary surgery.

OBSTETRICS AND GYNECOLOGY

Staff. Gynecological operations.

ORTHOPEDIC SURGERY

Staff. Dry clinics.

*Tuesday*

GENERAL SURGERY

R. B. BETTMAN and DR. TANNENBAUM. Gall-bladder operations.
M. L. PARKER. Gastro-intestinal operations.
Staff. Operative and dry clinics: Gall-bladder disease.

OBSTETRICS AND GYNECOLOGY

Staff. Dry clinics.

ORTHOPEDIC SURGERY

Staff. Operations.
D. H. LEVINTHAL. Knee joint surgery.

*Wednesday*

GENERAL SURGERY

D. C. STRAUS. Thyroid operations.
N. CROHN. Hernia operations.
Staff. Operative and dry clinics: Thyroid surgery.

GENITO-URINARY SURGERY

Staff. Operative and dry clinics.

*Thursday*

GENERAL SURGERY

ALFRED A. STRAUSS and SIEGFRIED STRAUSS. Gastro-intestinal operations.
M. PERLOW. Peripheral vascular surgery.
Staff. Operative and dry clinics: Peripheral vascular disease; blood transfusions.

OBSTETRICS AND GYNECOLOGY

Staff. Gynecological operations.

NEUROSURGERY

ADRIEN VERBRUGGHEN—9. Dry clinic: Cerebellar tumors in children.
ADRIEN VERBRUGGHEN—2. Operations.

*Friday*

GENERAL SURGERY

L. ZIMMERMAN. Hernia operations.
S. GOLDBERG. Abdominal operations.

GENITO-URINARY SURGERY

Staff. Operative and dry clinics.

ORTHOPEDIC SURGERY

Staff. Operations.

THORACIC SURGERY

R. B. BETTMAN and DR. TANNENBAUM. Operations.

## CHICAGO MEMORIAL HOSPITAL

### *Monday*

GENERAL SURGERY

PETER S. CLARK, CHARLES J. DRUECK, ROBERT A. MELENDY, BENNETT R. PARKER, JOHN VAN PROHASKA, M. L. WEINSTEIN, LEO M. ZIMMERMAN, and GEORGE M. Landau—1. Operative and dry clinic.

JOHN VAN PROHASKA. Surgical aspects of carcinoma of ampulla of Vater; enterogenous cysts in infants.

M. L. WEINSTEIN. Resection of stomach without clamps; rectal anesthesia.

LEO M. ZIMMERMAN. Essential problems in the surgical treatment of inguinal hernia.

BENNETT R. PARKER. Problems in gall-bladder surgery.

### *Tuesday*

FRACTURES AND OTHER TRAUMAS

T. C. BROWNING, EDWARD L. COMPERE, ARTHUR H. CONLEY, EMILE C. DUVAL, C. R. G. FORRESTER, A. H. MASON, FRED M. MILLER, S. PERRY ROGERS, HORACE STIMSON, and GEORGE M. LANDAU—9. Operative and dry clinic.

C. R. G. FORRESTER. Shoulder fractures.

A. H. MASON. Fractures of the scaphoid.

FRED M. MILLER and T. C. BROWNING. Fractures of foot and ankle.

EDWARD L. COMPERE. Vitamin D and calcium in fracture repair.

S. PERRY ROGERS. Vitallium in fractures.

EMILE C. DUVAL. Internal semilunar cartilage as a factor in industrial surgery.

HORACE STIMSON. Treatment of fractures of spine.

OPHTHALMOLOGY

FRANCIS M. CRAGE, HERMAN P. DAVIDSON, and GLENWAY NETHERCUT—2. Operative and dry clinic.

OTOLARYNGOLOGY

OSCAR CLEFF, ALFRED LEWY, ROBERT LEWY, JAMES B. MCBEAN, GORDON H. SCOTT, and RICHARD W. WATKINS—2. Operations.

### *Wednesday*

GENERAL SURGERY

Medical, surgical, x-ray and pathological departments—2. Symposia: Treatment of pneumonia with serum and sulfapyridine; peptic ulcer.

OBSTETRICS AND GYNECOLOGY

HARRY B. W. BENARON, JAMES E. FITZGERALD, WILLIAM F. HEWITT, GEORGE N. SCHIFF, BEATRICE E. TUCKER, and HARRY L. MEYERS—9. Operative and dry clinic.

HARRY B. W. BENARON. Presacral block in obstetrics.

GEORGE N. SCHIFF. Obstetrical analgesia.

JAMES E. FITZGERALD. Effect of Vitamin K in labor.

BEATRICE E. TUCKER and HARRY L. MEYERS. Manchester anterior colporrhaphy and perineorrhaphy.

### *Thursday*

GENERAL SURGERY

CASPER M. EPSTEIN—9. Operative clinic: Correction of cleft palate; facial plastic.

GENITO-URINARY SURGERY

VINCENT J. O'CONOR, JOHN P. O'NEIL, J. WILLIAM PARKER, and KENNETH SOKOL—9. Operative and dry clinic.

## EVANSTON HOSPITAL

### *Tuesday*

GENERAL SURGERY

W. R. PARKES, FREDERICK CHRISTOPHER, W. KENNETH JENNINGS, JAMES M. GRIER, and J. E. KEARNS—9. Operations.

OBSTETRICS AND GYNECOLOGY

W. C. DANFORTH, R. M. GRIER, HOWARD J. HOLLOWAY, P. H. SMITH, and C. H. GALLOWAY—9. Operations.

GENITO-URINARY SURGERY

JAMES I. FARRELL—9. Operations.

FRACTURES AND OTHER TRAUMAS

MARCUS H. HOBART and DWIGHT F. CLARK—9. Operations.

ORTHOPEDIC SURGERY

R. C. LONERGAN—9. Operations.

THORACIC SURGERY

JEROME R. HEAD—9. Operations.

OPHTHALMOLOGY

G. R. SOPER—9. Operations.

OTOLARYNGOLOGY

T. C. GALLOWAY and H. C. BALLENGER—9. Operations.

## ALBERT MERRITT BILLINGS HOSPITAL

### *Tuesday*

GENERAL SURGERY

L. R. DRAGSTEDT and HILGER P. JENKINS—9. Operative and dry clinic.

### *Wednesday*

GENITO-URINARY SURGERY

CHARLES B. HUGGINS—9. Operative and dry clinic.

### *Thursday*

ORTHOPEDIC SURGERY

CLY H. HATCHER and DALLAS B. PHEMISTER—9. Operative and dry clinic.

### *Friday*

GENERAL SURGERY

ALEXANDER BRUNSCHWIG and WILLIAM E. ADAMS—9. Operative and dry clinic.

## CHICAGO LYING-IN HOSPITAL

### *Thursday*

OBSTETRICS AND GYNECOLOGY

FRED L. ADAIR and staff—9. Operations: Cesarean section, hysterectomy, etc. Dry clinics: Manikin demonstration, delivery room technique, etc.

## PRESBYTERIAN HOSPITAL

*Tuesday*

OBSTETRICS AND GYNECOLOGY

N. Sproat Heaney, Edward Allen, Fred O. Priest, Harry Boysen, and Aaron E. Kanter—9. Operative and dry clinic.

*Wednesday*

GENERAL SURGERY

Vernon C. David, Kellogg Speed, Harry A. Oberhelman, Edwin M. Miller, Carl B. Davis, Albert H. Montgomery, and R. K. Gilcrest—9. Operative and dry clinic.

*Thursday*

GENITO-URINARY SURGERY

Herman L. Kretschmer, Robert H. Herbst, Norris J. Heckel, and James W. Merricks—9. Operative and dry clinic.

## MT. SINAI HOSPITAL

*Friday*

GENERAL SURGERY

D. A. Willis—9. New type of hernioplasty.
E. I. Greene—9. Operative clinic.
V. L. Schrager and staff—9. Hernioplasty.
A. A. Strauss and S. Strauss—9. Surgery of the colon.
M. R. Guttman—9. Plastic surgery of the nose.
J. Lifschutz—9. Endoscopy.
Emil Aison—9. Oral surgery.
J. M. Mora—9. Thyroidectomy.

OBSTETRICS AND GYNECOLOGY

A. E. Kanter and Louis Rudolph. Gynecological operations.
A. F. Lash. Vaginal hysterectomy.
H. Buxbaum, C. Newburger, and A. H. Goldfine. Obstetrical clinic.

GENITO-URINARY SURGERY

H. C. Rolnick—9. Operations.

ORTHOPEDIC SURGERY

C. L. Jacobs and Leo Miller—9. Operations.

OTOLARYNGOLOGY

S. Morwitz—9. Operations.

## ST. MARY OF NAZARETH HOSPITAL

*Days to be Announced*

GENERAL SURGERY

George M. Mueller, A. Sampolinski, E. Warszewski, and T. Steinert. Operative clinic.
T. Larkowski. Operative clinic: Paradural anesthesia.

OBSTETRICS AND GYNECOLOGY

M. Uznanski. Operations.

ORTHOPEDIC SURGERY

L. Czaja. Operations.

OTOLARYNGOLOGY

F. Piszkiewicz. Otological operations.

## WESLEY MEMORIAL HOSPITAL

*Tuesday*

GENERAL SURGERY

R. W. McNealy—9. Operative and dry clinic.

OBSTETRICS AND GYNECOLOGY

Charles B. Reed—9. Operative and dry clinic.

GENITO-URINARY SURGERY

Victor D. Lespinasse—9. Operative and dry clinic.

ORTHOPEDIC SURGERY

Philip H. Kreuscher—9. Operative and dry clinic.

THORACIC SURGERY

Earl O. Latimer—9. Operative and dry clinic.

OPHTHALMOLOGY

William A. Mann—9. Operative and dry clinic.

OTOLARYNGOLOGY

Thomas P. O'Connor—9. Operative and dry clinic.

## NORWEGIAN-AMERICAN HOSPITAL

*Thursday*

GENERAL SURGERY

J. M. Amberson—9. Postoperative intravenous medication.
G. B. Fauley—9:30. Surgical physiology of the thyroid.
A. M. Jensen—9:30. Sulfanilamide in general surgery.
J. R. Orndorff—10. Technique of thyroidectomy.
F. H. Fowler—10. Time question in appendicitis.
J. V. Fowler, Jr.—10:30. Pre-operative and postoperative care of the thyroid patient.
J. E. Verhaag—10:30. Hernia from industrial causes.
M. M. Corbett—10:30. Immediate treatment of abdominal injuries.
W. Johnson—11. Carcinoma of the stomach.
F. M. Nicholson—11. Treatment of scalp injuries.
M. E. Lichtenstein—11:30. Technique of cholecystectomy.
J. V. Fowler, Sr.—11:30. Carcinoma of the breast.

OBSTETRICS AND GYNECOLOGY

B. W. Breister—9. Indications for cesarean section.
P. F. Snyder—11. Differential diagnosis of uterine tumors.

GENITO-URINARY SURGERY

D. F. Rudnick—10. Electrical resection of the prostate.

FRACTURES AND OTHER TRAUMAS

H. A. Sofield—11. Steel pin fixation of fractures of neck of the femur.

OTOLARYNGOLOGY

M. A. Glatt—9. Control of hemorrhage in tonsillectomy.
J. W. Harned—9:30. Danger signals in mastoid infection.

## MOTHER CABRINI MEMORIAL HOSPITAL

*Wednesday*

GENERAL SURGERY

S. Chesrow and staff—9. Abdominal operations.

## PASSAVANT MEMORIAL HOSPITAL

### *Thursday*

GENERAL SURGERY

JOHN A. WOLFER and associates—9. Tumor clinic:
FRANK QUEEN. The surgeon and pathologist as a diagnostic team, i.e., the decision for and conduct of the biopsy, with illustrative cases.
EARL BARTH. Preliminaries that must not be forgotten prior to beginning x-ray therapy.
H. E. DAVIS. The selection of tumor cases and x-ray vs. radium therapy.
HENRY JAFFE. How much radiation therapy should malignant tumors receive? How should it be administered?
FRED MERRIFIELD. Surgical results with intra-oral cancers.
J. M. GREENE. Useful aids in the differential diagnosis of tumors of the neck.
JOHN MOHARDT. Our results with cancer of the breast.
E. M. SMITH, JR. Results with treatment of unusual cutaneous tumors.
JOHN DELPH. Cancer of the larynx.
L. L. VESEEN. The treatment of cancer of the male genitalia.
GEORGE GARDNER. The treatment of cancer of the female genitalia.
HERMAN CHOR. The psychiatrist's part in a tumor clinic; illustrative cases.
EARL BARTH. Tour of radiation therapy department of Northwestern University Medical School.

### *Days to Be Announced*

GENERAL SURGERY

J. R. BUCHBINDER. Presentation of cases illustrating gastric and thyroid surgery.
SUMNER L. KOCH, MICHAEL L. MASON, and HARVEY ALLEN. Problems in surgery of the hand.

OBSTETRICS AND GYNECOLOGY

ARTHUR H. CURTIS, GEORGE H. GARDNER and associates. Integration of newer anatomical studies with clinical gynecology.
DAVID HILLIS and associates. Presentation of obstetrical problems.

ORTHOPEDIC SURGERY

PAUL B. MAGNUSON, JAMES K. STACK, and FRANK E. STINCHFIELD. Cases illustrating results of joint débridement.
EMIL HAUSER. Presentation of cases showing end-results in certain orthopedic procedures.

NEUROSURGERY

LOYAL DAVIS and JOHN MARTIN. Presentation of cases.

GENITO-URINARY SURGERY

L. W. RIBA. Female urethritis, case presentations.

OPHTHALMOLOGY

SANFORD GIFFORD and associates. Presentation of problems.

OTOLARYNGOLOGY

JOHN F. DELPH and associates. Presentation of cases.

## ILLINOIS EYE AND EAR INFIRMARY

### *Monday*

OTOLARYNGOLOGY

SAMUEL SALINGER—2. Operative and dry clinic: Plastic surgery about the nose.

### *Tuesday*

OPHTHALMOLOGY

THOMAS D. ALLEN, V. M. LEECH, and G. W. NETHERCUT—2. Operative clinic: Cataracts; ptosis; glaucoma.

OTOLARYNGOLOGY

PHILIP O'CONNOR—9. Plastic surgery, demonstration of patients, lantern slides, etc.
CARL CHRISTOPH—9. Operative clinic: Radical mastoid.
E. J. BLONDER—2. Labyrinthine diagnosis and demonstration of the galvanic following reaction.
M. A. GLATT—2. Operative clinic: Radical mastoid and external frontal.

### *Wednesday*

OPHTHALMOLOGY

PETER KRONFELD—9. Gonioscopy.
KATHARINE CHAPMAN—9. Orthoptic clinic.
ROBERT VON DER HEYDT—3. Slit lamp demonstration.

OTOLARYNGOLOGY

DR. WOODRUFF—Laryngeal sinus and ear cases; endoral mastoid and sinus surgery.
PHILIP O'CONNOR—2. Operative clinic.

### *Thursday*

OPHTHALMOLOGY

LOUIS G. HOFFMAN—9. Operative and dry clinic: Verhoeff suture.
E. K. FINDLAY—10. Dry clinic.
E. K. FINDLAY—2. Operative clinic.

OTOLARYNGOLOGY

E. J. BLONDER—9. Operative and dry clinic: Radical mastoid.
M. A. GLATT—2. Osteomyelitis of the frontal bone.

### *Friday*

OPHTHALMOLOGY

PETER KRONFELD—9. Gonioscopy.
KATHARINE CHAPMAN—9. Orthoptics.
SAMUEL J. MEYER—2. Operative clinic: Cataracts; glaucoma.

OTOLARYNGOLOGY

ALFRED LEWY—2. Operative clinic.

## WOMEN AND CHILDREN'S HOSPITAL

### *Wednesday*

OBSTETRICS AND GYNECOLOGY

AMELIA GIRYOTAS, ELOISE PARSONS, PEARL STETLER, MARY EDITH WILLIAMS, and MAUDE HALL WINNETT—9. Surgical and gynecological operations.
BEATRICE TUCKER—9. Operations.
BERTHA VAN HOOSEN—9. Demonstration: Teaching gynecology by models.

## VETERANS ADMINISTRATION FACILITY

### *Wednesday*

GENERAL SURGERY

B. F. WARD—9. Operations.
R. B. MORELAND—9. Operative clinic: Tumors.
A. E. WILLIAMS—9. Inspection of deep x-ray and radium unit.
G. R. ALLABEN—10. Dry clinic: Diagnosis and treatment of certain types of malignant disease.
MAX CUTLER—11. Intra-oral and laryngeal malignancies.

GENITO-URINARY SURGERY

T. G. MCDOUGALL—9. Operations.

THORACIC SURGERY

JEROME R. HEAD—11. Dry clinic: Thoracoplasties.

## ILLINOIS MASONIC HOSPITAL

### *Thursday*

GENERAL SURGERY

H. W. MILLER and WALTER C. BORNEMEIER—9. Use of the peritoneoscope.
C. J. DRUECK, SR., and H. E. OLIVER—9. Colon operation.
T. G. WALLIN—9. Gall-bladder surgery.
R. B. MALCOLM—9. Surgery of the neck.
W. B. GERHARD—9. Gastric surgery.

OBSTETRICS AND GYNECOLOGY

F. O. BOWE and BEULAH WALLIN—9. Obstetrical clinic.

GENITO-URINARY SURGERY

C. O. RITCH and C. C. SAELHOF—9. Operations.
EDWARD WHITE and CHARLES MURRY—9. Pyelonephrectomy; prostatic surgery.

ORTHOPEDIC SURGERY

WALTER R. FISCHER and CHARLES N. PEASE—9. Clinic.

THORACIC SURGERY

MINAS JOANNIDES and W. E. KEESEY—9. Chest surgery.
MINAS JOANNIDES and LOUIS J. MILLER—9. Monodal drainage; extrapleural pneumolysis; phrenic neurectomy; anterior thoracoplasty.
LOUIS J. MILLER—9. Surgical aspects of pulmonary abscess; primary carcinoma of lungs, diagnostic and surgical aspects.

OTOLARYNGOLOGY

M. H. COTTLE and A. H. GEIGER—9. Mastoid operation.
A. H. GEIGER, M. H. COTTLE and H. E. TAYLOR—9. Local and general anesthesia in ear, nose and throat surgery.

## JACKSON PARK HOSPITAL

### *Wednesday*

GENERAL SURGERY

C. C. CLARK—9. Abdominal operations.
A. BAMBERGER—10. Abdominal and thyroid operations.
H. H. COX—10. Operative and dry clinic.

FRACTURES AND OTHER TRAUMAS

F. G. MURPHY—9. Operations.

OTOLARYNGOLOGY

NOAH FOX—9. Operations.

## MUNICIPAL TUBERCULOSIS SANITARIUM

### *Tuesday*

GENERAL SURGERY

CLEMENT MARTIN—9. Anorectal tuberculosis.

### *Wednesday*

GENITO-URINARY SURGERY

DORRIN RUDNICK—9. Genito-urinary tuberculosis.

### *Thursday*

GENERAL SURGERY

RICHARD DAVISON—9. Surgical treatment of tuberculosis.

OTOLARYNGOLOGY

GEORGE HOLMES—2. Bronchoscopy in tuberculosis.

### *Friday*

THORACIC SURGERY

MINAS JOANNIDES—9. Collapse therapy clinic.

## HOLY CROSS HOSPITAL

### *Days to Be Announced*

GENERAL SURGERY

V. F. TORCZYNSKI. Blood pressure and spinal anesthesia—study of 100 cases.
J. B. KARR. Injection treatment of hernia; herniotomy.
F. F. FRAIDER and N. B. PAVLETIC. Indirect inguinal hernia.
F. SALETTA. Thyroidectomy.
M. BADZMIEROWSKI. Thyroidectomy.
J. F. RUZIC and D. S. DICIRO. Hernioplasty; vaginal hysterectomies; cholecystectomy; common duct exploration; thyroidectomy.

OBSTETRICS AND GYNECOLOGY

P. E. LAWLER. Manikin demonstration.
F. F. FRAIDER and N. B. PAVLETIC. Hysterectomy.
F. SALETTA. Hysterectomy.

ORTHOPEDIC SURGERY

C. P. GALANTI. Rare bone tumors.

## WASHINGTON BOULEVARD HOSPITAL

### *Tuesday*

FRACTURES AND OTHER TRAUMAS

ARTHUR R. METZ—9. Operative and dry clinic.

### *Wednesday*

OBSTETRICS AND GYNECOLOGY

PAUL FOX—9. Operations.

### *Thursday*

GENITO-URINARY SURGERY

VINCENT J. O'CONOR—9. Operations.

## SWEDISH COVENANT HOSPITAL

*Wednesday*

GENERAL SURGERY

R. F. ELMER, W. B. STROMBERG, and A. C. PETERSON—9. Operative clinic: Surgery of stomach and gall tracts.
K. L. VEHE, A. P. SANDAHL, and R. E. TALBOTT—9. Head and neck infections; anatomical demonstrations.
M. R. BROMAN—9. Problems in pathology in a private hospital.
R. G. WILLY—9. Diagnostic problems studied in a private hospital.

OBSTETRICS AND GYNECOLOGY

R. A. LIFVENDAHL, G. F. HIBBERT, G. L. ROSENE, and H. J. TIMERMAN—9. Vaginal hysterectomy; cesarean section case studies.

GENITO-URINARY SURGERY

B. E. FILLIS, J. T. GERNON, and K. D. KOHLSTEDT—9. Genito-urinary problems.

FRACTURES AND OTHER TRAUMAS

O. T. ROBERG and O. T. ROBERG, JR.—9. Fractures.

OPHTHALMOLOGY

R. A. DAVIS—9. Operative and dry clinic: Glaucoma.

## ST. ANNE'S HOSPITAL

*Wednesday*

GENERAL SURGERY

G. F. THOMPSON, J. J. GEARIN, John L. KNAPP, JOHN W. KEENE, ADOLPH KRAFT, and H. M. PETERSON—1. Operations.

OBSTETRICS AND GYNECOLOGY

J. L. FLEMING and R. J. HAWKINS—3. Operations.

GENITO-URINARY SURGERY

H. J. DOOLEY—9. Operations.

ORTHOPEDIC SURGERY

J. J. CALLAHAN—9. Operative and dry clinic: Shoulder injuries.
THOMAS E. MEANY—10. Operations.

OTOLARYNGOLOGY

J. W. HAYDEN—11. Operations.

## EVANGELICAL DEACONESS HOSPITAL

*Tuesday*

GENERAL SURGERY

W. C. BORNEMEIER—9. Cholecystectomy.
PAUL MORF—9. Bilateral herniotomy.
JOHN PERL—10. Partial gastrectomy.

OBSTETRICS AND GYNECOLOGY

FREDERICK BOWE—9. Cesarean section.
A. J. SCHOENBERG—9. Hysterectomy.
R. J. NEEF—10. Perineorrhaphy.
R. C. STEFFEN—11. Amputation of cervix.

OTOLARYNGOLOGY

JOHN BICK—9. Tonsillectomy.
ARTHUR GEIGER—10. Deviated septum.

## HOSPITAL OF ST. ANTHONY DE PADUA

*Day to Be Announced*

GENERAL SURGERY

FRANK OLENTINE. Thyroid operations.
J. J. SPRAFKA. Abdominal operations.
S. E. DONLON, FRED EHRMANN, W. H. BRADLLY, JOSEPH ZABOKRTSKY, FRANK JIRKA, R. C. DRURY, H. P. SULLIVAN, and M. J. BADZMIEROWSKI. Operative and dry clinic.

OBSTETRICS AND GYNECOLOGY

M. A. WEISSKOPF. Obstetrical operations.

GENITO-URINARY SURGERY

OTTO JIRSA. Operations.

FRACTURES AND OTHER TRAUMAS

F. W. SLOBE. Traumatic surgery.

## COLUMBUS HOSPITAL

*Thursday*

GENERAL SURGERY

DANIEL A. ORTH—9. Operations.
H. E. DAVIS—9. Selective radiation therapy of malignancies; presentation of cases.
H. R. KENNY—10. Crohn's disease; presentation of cases.

OBSTETRICS AND GYNECOLOGY

CHANNING BARRETT—9. Operations.

GENITO-URINARY SURGERY

WILLIAM H. GEHL—9. Transurethral prostatic resection.

FRACTURES AND OTHER TRAUMAS

GEORGE BEECHER—9. Dry clinic.

ORTHOPEDIC SURGERY

FREDERICK MUELLER—9:30. Dry clinic.

OPHTHALMOLOGY

MICHAEL GOLDENBURG—9. Operations.

## ST. JOSEPH HOSPITAL

*Tuesday*

GENERAL SURGERY

Staff—9. Dry clinic: Gall-bladder surgery.

OBSTETRICS AND GYNECOLOGY

Staff—9. Gynecological dry clinic.

GENITO-URINARY SURGERY

Staff—9. Dry clinic.

ORTHOPEDIC SURGERY

Staff—9. Demonstrations: Lantern slides and moving pictures of fractures.

OPHTHALMOLOGY

Staff—9. Operative and dry clinic.

OTOLARYNGOLOGY

Staff—9. Operative and dry clinic.

## ST. BERNARD'S HOSPITAL

### *Wednesday*

GENERAL SURGERY

WILLIAM G. EPSTEIN—9. Thyroid operations.
L. B. DONKLE, G. CUSHING, and WILLIAM MULHOLLAND—9. Abdominal operations.
S. GOVERNALE—9. Dry clinic: Pseudohypertrophic muscular dystrophy.

GENITO-URINARY SURGERY

A. J. SULLIVAN—9. Prostatic operations.

OPHTHALMOLOGY

C. P. SULLIVAN—Cataract operations.

## ALEXIAN BROTHERS' HOSPITAL

### *Thursday*

GENERAL SURGERY

WILLIAM J. SWIFT—9. Herniotomy.
DANIEL MURPHY—9. Circulatory disturbances of lower extremity.
FREDERICK A. RETTIG—10. Abdominal surgery and post-operative care.

GENITO-URINARY SURGERY

JULIUS M. GLASSER—9. Prostatectomy, 2 cases.
EDWARD F. HESS—9. Dry clinic: Nephrotomy; cystoscopy and pyelography.
EDWARD W. WHITE—10. Prostatic electroresection; ureteral stone.
A. J. WOCHINSKI—10. Prostatic electroresection; fulguration of bladder tumor, 2 cases.

ORTHOPEDIC SURGERY

GEORGE L. APFELBACH—10. Demonstration of examination for lower back pain; non-union of neck of femur.

THORACIC SURGERY

MINAS JOANNIDES and LOUIS J. MILLER—9. Operative clinic: First-stage thoracoplasty; extrapleural pneumolysis, axillary approach; lobectomy for bronchiectasis. Dry clinic: Hedblom's syndrome, clinical and radiological aspects; chronic suppuration of the lung in relation to carcinoma of the lung.

## AUGUSTANA HOSPITAL

### *Tuesday*

GENERAL SURGERY

NELSON M. PERCY and OSCAR E. NADEAU—9. Operative and dry clinics.

### *Wednesday*

GENERAL SURGERY

A. T. LUNDGREN and EARL GARSIDE—9. Operative and dry clinics.
JOHN W. NUZUM and RUDOLPH ODEN—9. Operative and dry clinics.

### *Thursday*

GENERAL SURGERY

NELSON M. PERCY and OSCAR E. NADEAU—9. Operative and dry clinics.

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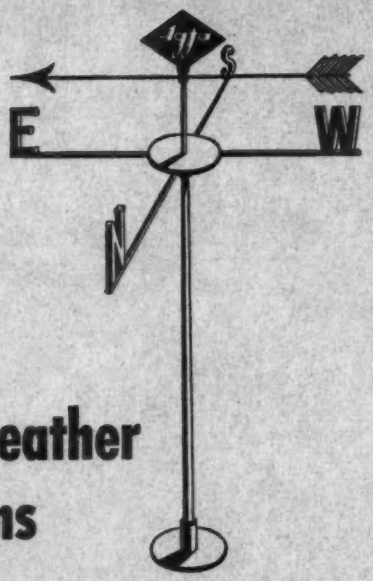
## With International Abstract of Surgery

VOLUME 70 June, 1940 NUMBER 6

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